UK. 11C1691 A. 0.4 [illegible]

ANESTHESIOLOGY CLINICS OF NORTH AMERICA

4

Jonathan L. Benumof, MD, *Consulting Editor*

VOLUME 6 / NUMBER 4
DECEMBER 1988

CARDIAC MONITORING

Paul G. Barash, MD, *Guest Editor*

W. B. SAUNDERS COMPANY
Harcourt Brace Jovanovich, Inc.

Philadelphia London Toronto
Montreal Sydney Tokyo

W. B. SAUNDERS COMPANY
Harcourt Brace Jovanovich, Inc.

The Curtis Center
Independence Square West
Philadelphia, PA 19106-3399

P24644

Anesthesiology Clinics of North America is covered in *Index Medicus, Current Contents, ISI/BIOMED*, and *Chemical Abstracts*.

ANESTHESIOLOGY CLINICS OF NORTH AMERICA ISSN 0889-8537
December 1988 Volume 6—Number 4

© 1988 by W. B. Saunders Company. Copyright under the Uniform Copyright Convention. Simultaneously published in Canada. All rights reserved. This book is protected by copyright. No part of it may be reproduced, stored in a retrieval system, or transmitted in any form or by any means, electronic, mechanical, photocopying, recording, or otherwise, without written permission from the publisher. Made in the United States of America.

Authorization to photocopy items for internal or personal use, or the internal or personal use of specific clients, is granted by W. B. Saunders Company for users registered with the Copyright Clearance Center (CCC) Transactional Reporting Service, provided that the base fee of $00.00 per copy, plus $.20 per page, is paid directly to CCC, 27 Congress St., Salem, MA 01970. For those organizations that have been granted a photocopy license by CCC, a separate system of payment has been arranged. The fee code for users of the Transactional Reporting Service is: 0899-8537/88 $0.00 + $.20.

The following information is published in accordance with the requirements of the United States Postal Code.

Anesthesiology Clinics of North America is published quarterly by W. B. Saunders Company, The Curtis Center, Independence Square West, Philadelphia, PA 19106-3399. Subscription price is $65.00 per year for individuals residing in the United States, $72.00 per year for foreign individuals, and $75.00 per year for institutions. Second class postage paid at Philadelphia, PA 19106, and additional mailing offices. There is a postage charge of $8.00 for subscriptions billed to U.S. addresses and shipped outside the U.S. POSTMASTER: Send address changes to W. B. Saunders Company, The Curtis Center, Independence Square West, Philadelphia, PA 19106-3399.

The editor of this publication is Margaret C. Burns, W. B. Saunders Company, The Curtis Center, Independence Square West, Philadelphia, PA 19106-3399.

Printed by the Maple-Vail Book Manufacturing Group, York, Pennsylvania.

Contributors

CORRIE ANDERSON, MD, Clinical Fellow in Anaesthesia, The Children's Hospital and Harvard Medical School, Boston, Massachusetts

GEORGE STEPHEN BAUSE, MD, MPH, Medical Curator, The Wood Library-Museum of Anesthesiology; Assistant Professor and Curator, The Yale Museum of Anesthesiology; Staff Anesthesiologist, West Haven V.A. Medical Center; Assistant Professor, Department of Anesthesiology, Yale University School of Medicine, New Haven, Connecticut

PATRICK E. CURLING, MD, Department of Anesthesiology, Yale University School of Medicine, New Haven, Connecticut

RICHARD I. HALL, MD, FRCP(C), Assistant Professor of Anaesthesia and Pharmacology, Dalhousie University and The Victoria General Hospital, Halifax, Nova Scotia, Canada

DOLLY DORIS HANSEN, MD, Assistant Professor of Anaesthesia, The Children's Hospital and Harvard Medical School, Boston, Massachusetts

PAUL ROBERT HICKEY, MD, Associate Professor of Anaesthesia, The Children's Hospital and Harvard Medical School, Boston, Massachusetts

ROBERTA HINES, MD, Assistant Professor of Anesthesiology, Director, Cardiothoracic Intensive Care Unit, Department of Anesthesiology, Yale University School of Medicine, Yale-New Haven Hospital, New Haven, Connecticut

J. C. HORROW, MD, Assistant Professor of Anesthesiology, Hahnemann University, Philadelphia, Pennsylvania

BRIAN R. JONES, MD, Chief Resident in Anesthesiology, University of California San Diego and Veterans Administration Medical Center, San Diego, California

KENNETH R. LaMANTIA, MD, Assistant Professor, Department of Anesthesiology, Yale University School of Medicine; Chief, Anesthesiology Service, West Haven Veterans Administration, New Haven, Connecticut

MARTIN J. LONDON, MD, Assistant Professor of Anesthesia, University of California, San Francisco, University of California Medical Center and Veterans Administration Medical Center, San Francisco, California

GERARD F. McCLOSKEY, MD, Department of Anesthesiology, Yale University School of Medicine, New Haven, Connecticut

DENNIS T. MANGANO, PhD, MD, Professor of Anesthesia, University of California, San Francisco, University of California Medical Center and Veterans Administration Medical Center, San Francisco, California

ROCCO MARANDO, MD, Assistant Professor, Department of Anesthesiology, Yale University School of Medicine; West Haven Veterans Administration Medical Center New Haven, Connecticut

EMERSON A. MOFFITT, MD, FRCP(C), Professor, Department of Anaesthesia, Dalhousie University and The Victoria General Hospital, Halifax, Nova Scotia, Canada

JAMES H. PHILIP, MD, Anesthesiologist and Director of Bioengineering, Department of Anesthesia, Brigham and Women's Hospital; Assistant Professor of Anaesthesiology, Harvard Medical School and Harvard-MIT Division of Health Sciences and Technology, Boston, Massachusetts

THEODORE JAY SANFORD, JR, MD, Associate Clinical Professor of Anesthesiology, University of California San Diego and Veterans Administration Medical Center, San Diego, California

ALAN J. SCHWARTZ, MD, MSED, Associate Dean of Academic Affairs, Professor of Anesthesiology, Hahnemann University Hospital, Philadelphia, Pennsylvania

DAVID T. SEITMAN, MD, Senior Instructor of Anesthesiology, Hahnemann University, Philadelphia, Pennsylvania

JOHN R. SLAVIK, MD, Assistant Professor, Department of Anesthesiology, Yale University School of Medicine, Yale-New Haven Hospital, New Haven, Connecticut

N. TY SMITH, MD, Professor of Anesthesiology, University of California San Diego and Veterans Administration Medical Center, San Diego, California

DANIEL M. THYS, MD, Associate Professor of Anesthesiology, Mount Sinai School of Medicine; Director, Division of Cardiothoracic Anesthesiology, Mount Sinai Hospital, New York, New York

JEFFERY S. VENDER, MD, Associate Professor, Clinical Anesthesia, Northwestern University Medical School, Chicago; Director, Intensive Care, Evanston Hospital, Evanston, Illinois

Contents

Preface xi

Paul G. Barash

An Historical Backdrop to Cardiovascular Monitoring 655

George Stephen Bause

Polarity, perfusion, and pulsation are recurring themes in the history of cardiovascular monitoring. Man has devised many philosophies and a host of instruments to help him understand and monitor his cardiovascular health.

Preoperative Cardiovascular Monitoring 683

Martin J. London and Dennis T. Mangano

A number of options are available for the preoperative screening of patients for risk factors predictive of postoperative cardiovascular morbidity. The application of 12-lead and ambulatory ST-segment electrocardiography, exercise stress testing, dipyridamole-thallium perfusion scanning, and determination of left ejection fraction by radionuclide angiography are reviewed along with implications of abnormal results for perioperative management. The presence of easily inducible myocardial ischemia, recent myocardial infarction, low ejection fraction, or poor exercise capacity place the patient at high risk. The selective and rational use of these tests allows the clinician to institute preoperative treatment of ischemia or congestive heart failure as well as aids in the choice of appropriate intraoperative and postoperative monitoring.

Electrical Safety and Device Calibration 699

J. C. Horrow and David T. Seitman

Proliferation of electrically powered devices in the operating room has required anesthesiologists to understand the principles governing electrical shock

and electrical safety. Knowledge of monitor calibration and monitor data processing techniques are equally important to ensure correct interpretation of the information these monitors provide.

Noninvasive Blood Pressure Measurement **721**

Theodore Jay Sanford, Jr, Brian R. Jones, and N. Ty Smith

This article examines several methods of measuring blood pressure noninvasively. The theories and clinical applications of each method are described. In addition, advantages and disadvantages of each are discussed.

Pulmonary Artery Catheter Monitoring **743**

Jeffery S. Vender

Since their introduction two decades ago, there has been a vast expansion in the clinical applications of pulmonary artery (PA) monitoring. Indicators for PA monitoring are broadly defined in the current medical textbooks. PA monitoring can help define the etiology of the clinical problem, monitor the pathophysiologic progression, and guide in the therapy as well as monitoring the responses to therapy. This article focuses on (1) the validity and interpretation of data obtained from PA pressure monitoring; (2) physical complications of PA monitoring; (3) thermodilution cardiac output; (4) mixed venous oxygen saturation monitoring; and (5) clinical application of PA catheters.

Perioperative Echocardiography **769**

John R. Slavik

Echocardiography is assuming an ever greater role in the preoperative and intraoperative assessment of myocardial function. Global and regional myocardial contraction patterns may be monitored. The effects of therapeutic or pharmacologic intervention on myocardial function can also be determined. In addition, intracardiac air can be reliably detected and measures taken early to prevent massive air embolism. Finally, the use of echocardiography may obviate the need for cardiac catheterization prior to heart surgery in selected patients.

Doppler Echocardiography **785**

Kenneth R. LaMantia

Velocity measurements by devices using the Doppler principle have recently increased in importance in

anesthesiology and critical care. Increased interest in noninvasive physiologic monitors has promoted the development of sophisticated devices to assess blood flow velocity. Advances in electronic instrumentation have allowed the production of smaller transducers capable of placement into previously inaccessible locations. This article focuses on the use of the Doppler principle to measure blood flow in the heart and great vessels and the importance of such measurements in diagnosing disease, monitoring physiologic function, and guiding therapy with emphasis on disease states commonly encountered by the anesthesiologist.

Cardiac Output 803

Daniel M. Thys

The measurement of cardiac output by the direct Fick method could again become a technique of interest because of widespread availability of mass spectrometry and continuous hemoglobin oximetry. The accuracy and reproducibility of the thermodilution technique are not great. Errors will occur when indicator is lost or gained, while an inconsistent injection technique will produce variability in the results. In the thoracic electrical impedance method, cardiac output is measured by sets of electrodes placed around the neck and lower thorax. The latest bioimpedance equipment incorporates new equations that have increased the accuracy of the technique.

Cardiovascular Monitoring for the Pediatric Patient: What's Appropriate? 825

Paul Robert Hickey, Dolly Doris Hansen, and Corrie Anderson

The available spectrum of cardiovascular monitoring for the pediatric patient is surveyed, along with the associated risks and benefits of each available pediatric monitoring modality. The disease states in children in which each form of monitoring is particularly appropriate are pointed out, along with the shortcomings of each type of monitoring. Reports of clinical experience and complications are included whenever these are available.

Monitoring the Coronary Circulation 839

Richard I. Hall and Emerson A. Moffitt

Two methods are currently employed to monitor changes in the coronary circulation. The coronary sinus catheter is used to measure global changes in flow and myocardial metabolism while radioisotope flow techniques measure changes in flow to ischemic areas of the myocardium. The advantages and disadvantages of each method are discussed.

Monitoring Right Ventricular Function **851**

Roberta Hines

An increased awareness of the importance of right ventricular (RV) function in governing overall myocardial performance has recently developed. As a result, more attention has now become focused on employing techniques aimed at monitoring RV function. Of particular interest to the anesthesiologist is the ability to diagnosis RV ischemia and infarction during the perioperative period.

Monitoring Intravenous Infusion and the Venous Circulation **865**

James H. Philip

Recent laboratory tests and limited patient studies have given us new insights into intravenous (IV) fluid administration and the venous circulation. These insights show that the laws of physics that are familiar in other situations also apply when fluid is infused through IV systems into patients. Our new insights provide a physical and mathematical model that describes how pressure, resistance, and flow are related in IV fluid administration.

The Physiologic Basis of Cardiovascular Monitoring **891**

Rocco Marando and Alan J. Schwartz

In the perioperative period, cardiovascular performance is evaluated, by both invasive and noninvasive monitors. The information gained from these devices is complementary. To effectively use the myriad cardiovascular monitors, a thorough understanding of the advantages and limitations of each of the cardiovascular measurements is essential. This article emphasizes the physiologic foundation of modern cardiovascular monitoring and the clinical application of commonly employed indices to assess left ventricular function.

Electrocardiography **903**

Gerard F. McCloskey and Patrick E. Curling

Electrocardiography has long been used for the detection of intraoperative dysrythmias and myocardial ischemia. The specifics of calibration, lead system selection, and electrical filtration for maximum sensi-

tivity in dysrythmia and ischemia detection are detailed. The configuration of the standard limb leads, augmented unipolar leads, and precordial unipolar leads are defined. In addition, several modified bipolar leads are discussed, and their sensitivity to ischemia versus dysrythmias are compared. Intracardiac, esophageal, and tracheal electrodes are also described, and their advantages and inherent dangers discussed. The intraoperative detection of myocardial ischemia, the characteristic ECG changes, and some unusual manifestations of ischemia are noted. Finally, newer computer-assisted electrocardiographic systems for automatic dysrythmia detection and improved ischemia monitoring including correlation analysis and ST-trend analysis are discussed.

Cumulative Index 1988 .... **917**

Subscription Information .... **Inside back cover**

RECENT ISSUES

September 1988

Myocardial Ischemia and Perioperative Infarction
J. G. Reves, MD, *Guest Editor*

June 1988

New Anesthetic Drugs
Robert J. Fragen, MD, *Guest Editor*

March 1988

Management of Patients with Multisystem Organ Failure
Vladimir Kvetan, MD, and Jeffrey Askanazi, *Guest Editors*

December 1987

Positive Airway Pressure Therapy: PPV and PEEP
Barry A. Shapiro, MD, and Roy D. Cane, MD, *Guest Editors*

FORTHCOMING ISSUES

March 1989

Management of Postoperative Pain
Rollin Oden, MD, *Guest Editor*

June 1989

Diagnosis and Management of Intraoperative Arrhythmias
Stephen Thomas, MD, *Guest Editor*

September 1989

Anesthesia and New Operations
A. Scott Wheeler, MD, *Guest Editor*

Preface

Paul G. Barash, MD
Guest Editor

Monitoring, an extension of the physical examination, is an integral component of the clinical practice of anesthesiology. More than 100 years ago, Snow reported that pulse rate, in addition to respiration, was required to assess the depth of anesthesia. However, it was not until the beginning of the twentieth century that Codman and Cushing advocated the measurement of heart rate and blood pressure, obtained on a regular basis (every 5 minutes) to adequately monitor patients receiving an ether anesthetic. Despite these early advances, monitoring of the cardiovascular system remained quite rudimentary. As late as 1969, some authorities even questioned the value of the intraoperative electrocardiogram.[8] More recently, standards have been promulgated for the minimal level of monitoring required for all patients. These standards are not comprehensive, but serve to reduce the risk of untoward events for which the cardiovascular and central nervous systems are final common pathways.

Cardiovascular monitoring facilitates the diagnosis and treatment of complex hemodynamic abnormalities. These can be categorized in terms of pump function, intravascular volume, and vascular resistance. Conservative clinicians may argue that experience and astute physical examination are adequate to diagnose and treat these derangements. However, routine clinical assessment has proved to be a poor predictor of the patient's hemodynamic status.[3,5]

The 1970s can be characterized as the "decade of invasive monitoring." Although the benefits of these techniques are important for patient care, limitations are obvious. The risks associated with invasive monitoring pose a significant hazard to the critically ill patient. Further, the use of invasive monitoring of cardiac performance (for example, PCWP) is based on the assumption that pressure measurement is a good approximation of ventricular volume status. Erroneous conclusions based on this notion of hemodynamic performance may result.[6]

In contrast, noninvasive assessment of cardiovascular function offers the anesthesiologist techniques that overcome these limita-

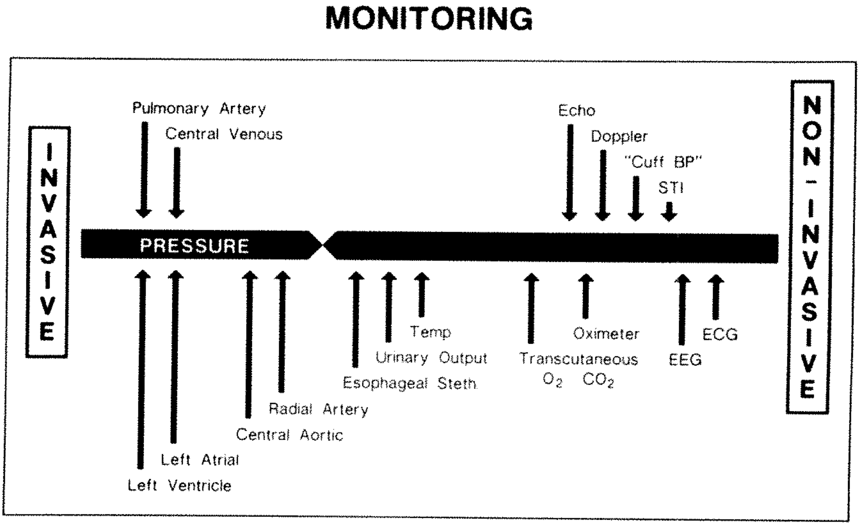


Figure 1. The monitoring spectrum of invasive to noninvasive devices. STI = systolic time intervals.

tions. The potential appeal of these methods is a more precise physiologic definition of the status of the cardiovascular system, without exposing the patient to risks of invasive examination. The graphic presentation of certain imaging techniques, for example, echocardiography, also serves as an excellent method to learn cardiovascular physiology. Thus, as we enter the twenty-first century, the anesthesiologist has a spectrum of cardiovascular monitors from which to choose (Fig. 1).

Many argue that due to improved monitoring techniques there has been a significant decrease in anesthetic-related mortality. It has also been hypothesized that more extensive use of monitors has had a positive impact on the cost of malpractice insurance premiums.[9] However, we should not be lulled into a false sense of security. As monitors and monitoring become more complex, the clinician's attention may be diverted from the patient. In an analogous situation, Dr. John Lauber (National Transportation Safety Board), commenting on airline accidents, stated, "Some recent incidents have convinced me that rather than eliminating human error, some of the new technology has resulted in the creation of new opportunities for entirely new categories of human error."[10]

With increasing frequency, we are being asked to justify the expense and risk of monitors. The cost-benefit ratio is difficult to apply in many clinical situations. At present, the pulmonary artery catheter (PAC) is the monitoring device under the most intense scrutiny. Owing to the absence of any prospective controlled studies, its use has engendered heated debate.[1,11] The difficulty in conducting such a scientific investigation is exemplified by the application of the PAC in cardiac surgical patients. If reduction in mortality rate from 1.5 to 0.75 per cent is to be used as an endpoint in a prospective controlled clinical trial, then approximately 3400 patients are required. The logistics and ethics of such a study preclude its implementation.

Although the use of a PAC may be considered too sophisticated an example for cost-benefit analysis, Cohen and colleagues posed an even more direct question: Does the use of monitors result in decreased nonfatal complication rates in anesthetized patients? They examined the records of 112,721 patients from a single hospital over a 9-year period.[2] Despite an increased use of monitors in the operating room, the cardiac arrest rate per 10,000 anesthetics did not decrease! A more striking example was the report of Lunn et al, who found that between 1972 and 1977, 18 per cent of patients who were administered anesthetics in England did not have blood pressure monitoring. More intriguing was the fact that 10 per cent of the anesthetics were administered without any monitoring.[7] Finally, Cooper et al reported that 3 per cent (15/507) of critical intraoperative incidents were directly related to misuse of a monitor and 27 per cent (19/70) of negative outcomes were associated with faulty monitoring.[4]

These disparate observations may puzzle and disturb the reader. The current issue of the *Anesthesiology Clinics of North America* brings together 23 contributors, who articulately discuss the place of a given monitor (or device) in clinical practice. The discerning reader will integrate the messages contained within each article to gain insight into their value, both in economic terms as well as in improved patient care.

REFERENCES

1. Bashein G, Ivey TD: Con: A pulmonary artery catheter is not indicated for all patients for coronary artery surgery. J Cardiothorac Anesth 1:362, 1987
2. Cohen MM, Duncan PG, Pope WDB, et al: A survey of 112,000 anaesthetics at one teaching hospital (1975–83). Can Anaesth Soc J 3:22–31, 1986
3. Connors AF, McCaffree DR, Gray BA: Evaluation of right heart catheterization in the critically ill patient without acute myocardial infarction. N Engl J Med 308:263–267, 1983
4. Cooper JB, Newbower RS, Long CD, et al: Preventable anesthesia mishaps: A study of human factors. Anesthesiology 49:399–406, 1978
5. Del Guercio LRM, Cohn JD: Monitoring operative risk in the elderly. JAMA 243:1350–1355, 1980
6. Hansen RM, Viquerat CE, Matthay MA, et al: Poor correlation between pulmonary arterial wedge pressure and left ventricular end diastolic volume after coronary artery bypass graft surgery. Anesthesiology 64:764–770, 1986
7. Lunn JN, Farrow SC, Fowkes FGR, et al: Epidemiology in anesthesia I: Anesthetic practice over 20 years. Br J Anaesth 54:503, 1982
8. Munson ES: Reports of scientific meetings: Monitoring the anesthetized patient. Anesthesiology 32:178, 1970

0889-8537/88 $0.00 + .20

An Historical Backdrop to Cardiovascular Monitoring

*George Stephen Bause, MD, MPH**

In attempting to monitor human health, early man perceived the physical world as a template for understanding himself and his peers. The warmth of living and the frigidity of dying were mirrored in the day and the night. Life and death were embodied, respectively, in the sun and the moon. The daily struggle for survival encouraged a view that life and death were antagonists. That struggle also created the practical knowledge of target areas for weapon strikes. Hunting lore taught prehistoric man that the center of the body—either the center of the thorax or the high abdomen—contained the secret of living. Indeed, the first anatomic illustration of the heart may be part of a red ochre drawing of a mammoth discovered in a Spanish cave at El Pindal.[70] A leaf-shaped dark area, the heart or vital (perhaps holy?) structure was depicted as shoulder-level in location. This secret of life or vital organ was recorded as early as the Paleolithic period on cave walls by hunters.

MESOPOTAMIAN FOCUS: THE LIVER

As the cradle of civilization, Mesopotamia witnessed the rise of the written record and of peoples capable of transmitting their thoughts on the secret of life to future cultures. Sumerian ideographic writing arranged in vertical columns from right-to-left eventually yielded to top-to-bottom rows of cuneiform from left-to-right. The introduction of clay tablets and stylets for records preserved the ideas of a people that viewed medicine as magical. Living in Mesopotamia ("between the rivers"), the Sumerian emphasis on fluids and flow were products of their proximity to the Tigris and Euphrates rivers. Blood was considered the carrier of all vital functions. As the collecting point of life fluids and blood, the liver was the seat of life. Con-

---

*Medical Curator, The Wood Library-Museum of Anesthesiology; Assistant Professor and Curator, The Yale Museum of Anesthesiology; Staff Anesthesiologist, West Haven V.A. Medical Center; Assistant Professor, Department of Anesthesiology, Yale University School of Medicine, New Haven, Connecticut

sequently, hepatoscopy, the inspection of livers of sacrificed animals, assumed a vital role in public affairs.

Hepatoscopy highlighted the Assyro-Babylonian practice of medicine. In the 21st verse of his 21st chapter, the prophet Ezekiel reported that "the King of Babylon stood at the parting of the way, at the head of the two ways, to use divination: he made his arrows bright, he consulted with images, he looked at the liver." The person seeking to learn his future would breathe upon a sacrificial animal, and the hepatoscopist would slay the animal and examine its liver. The hepatoscopist of Babylon evolved into the haruspex of Rome, who would divine the future of an empire by examining the liver and entrails of sacrificed animals. Gradually, right-handedness or having a large right lobe of the liver was regarded as "dexter" or auspicious; left-handedness, or a predominant left lobe, as "sinister." The special Babylonian caste that practiced medicine also plucked herbs by moonlight, another practice that would be continued for centuries to follow. Regarding seven as a magic, lunar-based number, the Babylonian practitioner would not provide patient care on the seventh day. Nonetheless, the Babylonian emphasis on counting and observation formed the sexagesimal basis of Assyro-Babylonian mathematics from which we derived our 60-minute hour and our 60-second minute. Babylonian observation and vigilance were incorporated into the rigid Code of Hammurabi, which provided harsh penalties to physicians whose patients experienced undesirable outcomes.

MESOAMERICAN FOCUS: THE HEART

Civilization developed many centuries later on the opposite hemisphere, when the Olmecs flourished in Mexico around 1250 BC. Successive Mesoamerican peoples flourished and declined including major Peruvian ones like the Chavin, Paracus, Tiahuanacan, and Incan cultures. The Olmecs were succeeded in Mexico by the Zapotecs and subsequently the Teotihuacan culture, which built a 20-story Pyramid of the Sun. Eventually, the Chichimec nomads roamed through Mexico, only to yield to the Mayans. A theocracy, Mayan culture was ruled by *hemenes* or priests, who wrote in hieroglyphics and formulated detailed calendars. The Toltecs and the Mixtecs preceded the great Mesoamerican culture of the Aztecs.

The Aztecs seem to have distilled many aspects of their predecessors into a complex social scheme. They constructed great pyramids and altars for sun worship. Unfortunately for their enemies, the Aztecs conducted astonishingly cruel human sacrifices, removing beating human hearts from their victims' chests with obsidian razors. Offerings of the heart and blood of their enemies to the sun-god suggest the central role that the heart, not the liver, played in Aztec society. In figurines from El Naranjo in Central Veracruz, the mythical and central role of the heart for Mesoamerican civilization is symbolized by the exposed heart seen in place of the umbilicus.

POLARITY

The prehistoric preoccupation with life and death was transformed by civilized man into a quest for the spark of life. What exactly was this life force? Man saw an energy in living and a vacuum in dying.

EGYPTIAN: ISIS/OSIRIS

The ancient Egyptians translated the great dual of life and death into a grand dualism of life and the afterlife. Unlike the Mesopotamians before or the Mesoamericans to follow, Egyptians discounted the role of blood as the carrier of life. Instead they postulated that air was the prime conveyor and that the heart was the vital organ. The rites of mummification and embalming provided the Egyptian with tremendous opportunity for understanding human anatomy. As a rule, the lungs, liver, stomach, and intestines were embalmed in separate stone canopic jars. The heart and major vessels were purposefully left in anatomic position for use in the afterlife. The Egyptian layman had a morbid fear that his heart might be damaged or stolen after death, and that he would be robbed of his afterlife.[40] The anonymous Egyptian author of the *Book of the Dead* pleads "Let not my heart be taken from me, let it not be wounded, and may neither swords nor gashes be dealt upon me because it hath been taken from me." Although Ra, the sun-god, was the supreme being, Egyptian life centered on the siblings Isis and Osiris. As the symbol of mother earth, Isis promoted healing and the sustenance of earthly life. Her brother Osiris was the Nile personified. Cruelly dismembered by Seth, Osiris was resuscitated and made whole by Isis' lying upon him. The great polarity of ancient Egyptian life and afterlife was symbolized by the sibling gods Isis and Osiris.[51] Their son Horus was blinded by Seth and healed by the physician to the gods, Thoth. The weeping eye of the suffering Horus became the symbol of godly protection and recovery. The eye of Horus is represented in modern times by the "Rx" on modern day prescriptions. In fact, the great secrecy of Egyptian prescriptions and potions was perpetuated into the Middle Ages as *alchemy*, a word derived from "chem," an ancient name for Egypt. The general magic and secrecy encouraged by the medical fraternity of old chem is further evidenced in *The Secret Book of the Physician*. Both the 17th century BC surgical treatise, the Edwin Smith Papyrus, and the potion-laden medical tract from 1550 BC, the Ebers Papyrus, probably shared a common source in *The Secret Book*. As the architect of the world's oldest free-standing structure, the Step-Pyramid at Saqqara, Imhotep is also credited with authoring *The Secret Book of the Physician* as early as 2650 BC.[51]

CHINESE: YIN/YANG

The ancient Chinese viewed the universe as t'ai chi: the "great ultimate" or "great circle." The purpose or pattern of this universe was embodied in tao, "the way." The oldest medical book extant, the *Huang Ti Nei Ching Su Wen*, contains su wen ("familiar conversations" or "simple questions") of the *Nei Ching* (Classic of Internal Medicine) attributed to Huang Ti (the Yellow Emperor). The Yellow Lord or Emperor Huang Ti (2697 to 2597 BC) was the third of China's first five emperors. The *Nei Ching* is thought to have been recorded on paper about 1000 BC following many centuries of oral tradition. The second book of the *Nei Ching* opens with a treatise on the interaction of the polar principles of Chinese thought: yin and yang.

> The principle of Yin and Yang (the male and female elements in nature) is the basic principle of the universe. It is the principle of everything in creation. It brings about the transformation to parenthood; it is the root and source of life and death; and it is also found within the temples of the gods.
>
> In order to treat and cure diseases one must search into their origin.
>
> Heaven was created by an accumulation of Yang, the element of light; Earth was created by an accumulation of Yin, the element of darkness.
>
> Yang stands for peace and serenity, Yin stands for recklessness and turmoil. Yang stands for destruction and Yin stands for conservation. Yang causes evaporation and Yin gives shape to things.
>
> Extreme cold brings forth intense heat (fever) and intense heat brings forth extreme cold (chills). Cold air generates mud and corruption; hot air generates clarity and honesty.
>
> If the air upon the earth is clear, then food is produced and eaten at leisure. If the air above is foul, it causes dropsical swellings.
>
> Through these interactions of their functions, Yin and Yang, the negative and positive principles in nature, are responsible for diseases which befall those who are rebellious to the laws of nature as well as those who conform to them.[92]

INDIAN: PITHA/KAPHA

In a fascinating parallel to the Chinese tao, yin, and yang, the Hindu trinity of gods featured the creator Brahma, the preserver Vishnu, and the destroyer Siva. Ayurvedic medicine evolved around the "three faults" or tridoshas: Vayu, Pitha, and Kapha.

> With reference to the polarity of these forces, Vayu or air represents the neutron, is the nerve force in the body, and splits up the atom into electrons and protons. Pitha or fire represents the electron and controls enzymes, the hormones, and the metabolic as well as the circulatory systems, all of which impart to the body heat necessary for its preservation and functioning. Kapha or water represents the proton, controls all the mucous surfaces of the body, and is similar to protoplasm.[1]

The Ayurvedic tradition postulates the existence of nerve force or energy and acknowledges the existence of negative Pitha and positive Kapha charges in the living organism.

GREEK: ODD/EVEN

With the possible exception of the Pythagorean school, the Ayurvedic insight into a life force and nervous energy was largely unrecognized by the ancient Greeks. Pythagoras (580 to 489 BC) started medical practice with a keen interest in procreation. This orientation may explain his cultivating a philosophy of numbers and a theory of harmony. The odd and the even were considered major Pythagorean principles of life and well-being. Indeed, the Pythagorean physician considered as numbered days the time course of each illness he attended. Perhaps the ultimate medical secret, the mystic rites of the Pythagoreans were translocated from Greece to Croton, Italy. For this reason, Aristotle referred to the Pythagoreans as the Italic School.

Aristotle had a much greater impact to make on man's search for a life force and for polarity in life. While describing the electric ray in 340 BC, Aristotle observed, "the torpedo narcotizes the creatures it wants to catch, overpowering them by the strength of a shock that is resident in its body. . . ."[16]

MODERN: NEGATIVE/POSITIVE

Two thousand years passed until Aristotle's observations on the torpedo kindled the interest of natural philosopher John Walsh.[97] In 1774 Walsh wrote to Benjamin Franklin that "the effect of the torpedo appears to be absolutely electrical, by forming its circuit through the same conductors with electricity, for instance metals and water; and by being intercepted by the same non-conductors, for example glass and sealing wax . . . the back and the breast of the animal [are] in different states of electricity."[98] These two states of electrical charge had, of course, been previously defined by America's first physicist, Benjamin Franklin. Glass rubbed by silk yielded what Franklin termed "positive" electrical charge. Hard rubber brushed by fur produced "negative" electrical charge.[83] Unfortunately, both Walsh and Franklin considered the electric ray merely a curiosity of nature.

However, a professor of anatomy at the University of Bologna, Aloysio Luigi Galvani (1737 to 1798) speculated that "animal electricity" occurred in all living tissues. He had noted in 1787 that pivoting a nearby electrostatic apparatus about a scalpel touching an exposed nerve on a frog's hind leg produced a contraction of the animal's leg. Eventually Galvani discovered that merely touching a nerve or muscle with a bimetallic rod would produce the same result: muscular contraction, reflecting electricity which Galvani believed to have been generated by the living tissues themselves.[48] Professor of physics at the University of Pavia, Alessandro Volta (1745 to 1827) considered Galvani to be "the frog's dancing master" and suggested that the muscle contraction resulted from electricity generated between dissimilar metals in the rod.[94] Publishing anonymously in 1794, Galvani simultaneously defined the current of injury and refuted Volta's assertion by showing contraction of muscle innervated by a nerve in contact with injured and uninjured tissue.[46] Volta's objections to animal electricity were ultimately silenced by his own voltaic pile. That invention led ironically to the discovery in 1820 by Hans Christian Oersted (1777 to 1851) of electromagnetism, the fundamental principle of the galvanometer.[78]

Indeed using a slow, homemade galvanometer in 1843, the founder of modern electrophysiology, Emil DuBois-Reymond (1818 to 1896), recorded the magnitude of the electric potential generated by frog muscle.[31] He referred to the action potential as "negative variation" after noticing its diminution after repeated stimulation. Unhappy with his homemade galvanometer, DuBois-Reymond interposed a two-position switch in the instrument such that a stimulus could be delivered by one position of the switch and interrupted by the other. Because he could now sample the magnitude of the electric potential over brief time intervals, DuBois-Reymond named his 1849 device the "flow-slicer" or rheotome.[32] A pupil of his, Julius Bernstein (1839 to 1917) eventually designed a flow-slicer capable of varying the time interval between stimulating and sampling. Reported in 1868, Bernstein's "differential rheotome" produced the first electrocardiogram ever recorded.[7]

The next advance in pursuing animal electricity resulted from an experimental spill in Heidelberg of sulfuric acid on a drop of mercury which contracted when touched with an iron wire.[16] Gabriel Lippmann (1845 to 1921) recalled this experiment and realized that the changes in the electric potential altered the surface tension at the mercury/sulfuric acid interface. In 1872 Lippmann introduced the capillary electrometer, the first device sensitive enough to permit easy continuous recordings of action potential. Etienne-Jules Marey (1830 to 1904) of Paris added a photographic recorder to the capillary electrometer in 1876.[74] By 1887 the first human "electrogram" had been performed with a capillary electrometer by Augustus Desire Waller (1856 to 1922).[96] Waller demonstrated that the capillary electrometer could record cardiac variations in electrical potential from the surface of the body. Lecturing in 1888 at St. Mary's Hospital Medical School, London, Waller renamed his recordings "cardiograms."

EINTHOVEN: THE STRING GALVANOMETER

Despite these successes, the capillary electrometer's mercurial inertia produced a slow response time as well as overshooting once the mercurial mass was set in motion. A Java-born Dutchman named Willem Einthoven (1860 to 1927) attacked the problem of mercurial inertia with a bow and arrow. He eliminated mercury. Einthoven produced strings 7 μm in diameter by heating quartz fused to an archery arrow and launching the arrow from a drawn bow. To render a quartz string electrically conductive, he subsequently plated it with pure silver. Thus Einthoven produced a wire with little mass, to minimize inertia, and high electrical resistance.[34] For the galvanometer portion of his string galvanometer, Einthoven had to construct a constant, powerful electromagnet. Generating so much heat, Einthoven's 22,000 gauss electromagnet required a water-cooled jacket for heat removal. Filling two rooms in Leiden, Einthoven's first string electrocardiograph weighed 600 lb and required five people to operate it.[35]

The commercial value of the electrocardiograph rose as dysrhythmia detection became important for both atrial and ventricular fibrillation.[60,72] Charles Darwin's seventh and youngest child, Horace Darwin, directed the commercial research and development of the electrocardiograph by Cambridge Scientific Instrument (CSI) Co., Ltd., of Great Britain. The size and heat production of the electromagnet were reduced. Although the first electrocardiograph was sold by CSI in 1905, not until 1912 were the units of a size practical for use in a hospital diagnostic room. Replacing Einthoven's cathodic bombardment method for silvering the quartz strings, CSI adapted Charles Hindle's method by bombarding glass with gold ions.[17] The same year, 1918, that Bousfield published the first electrocardiograph during angina pectoris,[12] the first isolated uses of electrocardiography during surgery were reported:[85] Krumbhaar examined "toxic goiter"[62] and Heard and Strauss observed nodal rhythms.[58] CSI finally merged with Hindle in 1925 to form Cambridge Medical Instruments, and their new corporation produced the first portable electrocardiograph the following year.

Portability was crucial to popularizing use of electrocardiography in both the medical office and the surgical suite. A general practitioner from Providence, Rhode Island, Elihu Wing Smith (1884 to 1968) was a pioneer in encouraging the perioperative use of the electrocardiograph as early as 1927 (personal communication, Thomas Breen, October 1987). At this point in history, the electrocardiograph was a frustrating instrument, requiring both photographic development time and limited use because of the heat it generated. The latter fact may explain why Smith's first electrocardiograph has not been located: it may have been damaged by an ether explosion during intraoperative use. Smith became re-enamored with a later model electrocardiograph when it incorporated Lockhart's electrostethograph, which featured a "microphone . . . connected with the input of said amplifier and the output of said amplifier . . . connected with said galvanometer whereby vibrations picked up by the microphone [were] recorded on the film."[67] The "Simpli-Trol" Portable Model Cambridge Electrocardiograph was purchased by Smith in 1938 (Fig. 1). Though still hampered by delay time for photographic development, Smith continued recording preoperative and postoperative electrocardiograms in his private office in Providence (personal communication, Elihu Wing Smith, Jr, MD, December 1987). Little did Smith realize that his and others' advocacy of perioperative electrocardiography would lead to electrical isolation, cathode ray oscilloscopes, and to computerized rhythm and segment monitors.

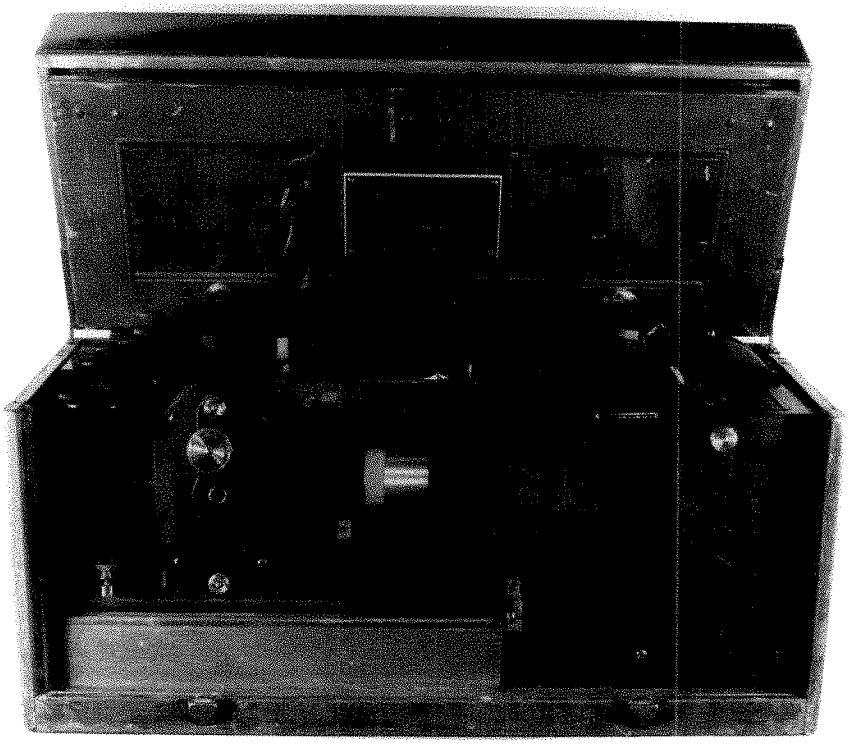


Figure 1. The "Simpli-Trol" Portable Model Cambridge Electrocardiograph used by Elihu Wing Smith, a pioneer of perioperative electrocardiography.

On the 25th anniversary of Einthoven's string electrocardiograph, the Russian electrophysiologist Samojloff begged Einthoven to read Samojloff's "letter to the string galvanometer, since it can write but not read." Einthoven responded:

> I have carried out precisely your request and read to the galvanometer your letter. Apparently he listened and took in with pleasure and joy, all that you wrote. He hadn't suspected that he had done so much for humanity, but at the place where you said he does not know how to read, he all of a sudden became furious, so that I and my family became even alarmed. He cried: 'What, I can't read? It's a terrible lie. Do I not read all the secrets of the heart?'[87]

From Imhotep's *Secret Book of the Physician* to Einthoven's "secrets of the heart," man searched philosophically for dualistic explanations for the spark of life. This quest for polarity evolved into a wonderful means of monitoring the very electricity of life.

PERFUSION

The Mesopotamian concept of life streaming inside the body's vessels was probably a product of life on the banks of the Tigris and

Euphrates rivers. As man sought to understand his body and the life flowing through it, he had to first distinguish the life conduits and whether these streamed with spirits, air, or blood. Eventually learning that he could hear the rush of life fluids within the vessels of his body, man discovered auscultation. To make this discovery, man needed first to comprehend what fluid flowed where and in what pattern (for example, ebb-and-flow or in circulation).

Egyptian Pneumatics

In the 9th year of the reign of Amenophis I, about 1550 BC, the Egyptians transcribed the Ebers Papyrus, which emphasized both the anatomy and physiology of the heart. The first five lines of the 99th column of the papyrus reveal:

> The beginning of the physician's secret: knowledge of the heart's movement and of the heart.
>
> There are vessels from it to every limb. As to this, when any physician, any surgeon (lit. Sachmet-priest) or anu exorcist applies the hands or his fingers to the head, to the back of the head, to the hands, to the place of the stomach, to the arms or to the feet, then he examines the heart, because all his limbs possess vessels, that is: it (the heart) speaks out of the vessels of every limb.[33]

Seven lines later, the Ebers Papyrus states: "As for the air that enters at the nose it enters to the heart and lungs, and they convey to the whole [body]." The pneumatic concept of life pervaded Egyptian thought.[18] Even bodies awaiting afterlife were left with "the opening of the mouth" in order to receive the spirit for afterlife. The sounds of pneumatic flow and the heartbeat could be transmitted audibly to the Egyptian physician. There is instruction in auscultation provided by the Ebers Papyrus: "Here the ear hears beneath. . . ."[33]

Chinese Vessels

The *Huang Ti Nei Ching Su Wen* states unequivocally that "All blood is under control of the heart. The heart regulates all blood of the body."[1] The ancient Chinese confused nerves, arteries, and veins, yet they clearly grasped some concepts of circulation. The *Nei Ching* observed that "The blood current flows continuously in a circle and never stops."[70]

Greek Distinctions

The empirical lay practice of Homeric medicine maintained that the diaphragm was the seat of life. One's soul escaped to Hades either by exsanguinating from wounds or via the nostrils with the last breath.

Contrast this view with that of Alcmaeon of Croton (f. 500 BC), who gave rise to the Grecian School of Cos. Alcmaeon asserted that the brain was the seat of senses and life; moreover, he distinguished veins from arteries.

The Greek anatomist Praxagoras (335 BC) formally distinguished arteries from veins. His disciple, Herophilus of Chalcedon (f. 315 BC) distinguished nerves from blood vessels. An Alexandrian, Erasistratus (c. 310 to 250 BC) hypothesized that blood moved from veins through small vessels (capillaries) into arteries—a reverse circulation of the blood!

Claudius Galen (138 to 201) was born in Pergamon, Asia Minor, near the site of an Aesculapian temple. He described three spirits of man: pneuma psychicon (animal spirit), pneuma zoticon (vital spirit), and pneuma physicon (natural spirit). Galen also declared that blood moved between the ventricles through invisible pores. Correctly identifying blood within the arteries, Galen theorized that blood ebbed and flowed. Arabian Galenists helped promulgate an understanding that the animal spirit was seated in the brain and conducted by the nerves; the natural spirit, in the liver, by the veins; and the vital spirit, in the heart, by the arteries.

Eastern Theories of Circulation

A Zoroastrian from southwestern Persia, Ali ibn Abbas Al-Majusi (Haly Abbas) collated his system of medicine, *The Royal*, for King Abudu'd-Dawla Fanakhusraw the Buwayhid (949 to 982). The first to conceive the existence of a capillary system, Haly Abbas suggested that pores existed between pulsating and nonpulsating vessels.[36]

That pores did not exist, interventricularly, was the contention of Ibn an-Nafis (c. 1210 to 1288). The chief medical officer of the Mansuri Hospital in Cairo, Ala ad-Din ibn an-Nafis al-Qurashi ad-Dimashqi challenged Galen's theory of interventricular pores.[54] Ibn an-Nafis countered, "There is no passage between these two cavities: for the substance of the heart is solid in this region and has neither a visible passage, as was thought by some persons, nor an invisible one which could have permitted the transmission of blood, as was alleged by Galen."[76] Beyond refuting Galen, Ibn an-Nafis registered the first clear statement of the lesser or pulmonary circulation: "Therefore, the blood, after having been refined, must rise in the arterious vein (pulmonary artery) to the lung in order to expand its volume and to be mixed with air so that its fumes and part may be clarified and may reach the venous artery (pulmonary vein) in which it is transmitted to the left cavity of the heart."[76]

Western Theories of Circulation

A Spanish physiologist-theologian, Miguel Serveto (1509 to 1553) of Villanueva de Sigena (Michael Servetus Villanovanus) sought the nature of God as revealed through man's soul and man's body. As the Spanish Inquisition terrorized his homeland, Serveto escaped to Paris and subsequently to tutorials under Gunther, Sylvius, and Vesalius.[23] Serveto developed his own theories on the pulmonary circulation, realizing that:

> a crimson color . . . is generated, as said, by the mingling of the inspired air with the more subtle portion of the blood which the right ventricle of the heart communicates to the left. This communication, however, does not take place

> through the septum, partition, or mid-wall of the heart, as commonly believed, but by another admirable contrivance, the blood being transmitted from the pulmonary artery (vena arteriosa) to the pulmonary vein (arteria venosa) by a long passage through the lungs, in the course of which it is elaborated, and becomes of a crimson color.[40,89]

Serveto was burned at the stake for his critical views on the pulmonary circulation.

Coining the term "circulation" (1569), Andrea Cesalpino (c. 1519 to 1603) of Arezzo, Tuscany, Italy, actually published his descriptions of the pulmonary and the systemic circulations some 57 years before William Harvey did so.[3] His anatomic dissections led him to conclude that:

> The circulation of the blood, which takes place from the right ventricle to the left ventricle, in passing through the lungs, agrees quite exactly with the following facts. . . . There are two vessels which end in the right ventricle, two in the left. One of the two is afferent, the other efferent. . . . The blood is conducted to the heart by the veins . . . is carried by the arteries throughout the body . . . the veins are engorged below a ligature, not above. Those who bleed patients are familiar with this experiment.[19,86]

Cesalpino also recognized the role of venous valves in maintaining circulation:

> The passages of the heart are so arranged by nature that from the vena cava a flow takes place into the right ventricle, whence the way is open into the lungs. From the lungs, moreover, there is another entrance into the left ventricle of the heart, from which then a way is open into the aorta artery, certain membranes being so placed at the mouths of the vessels that they prevent return. There is a kind of perpetual movement through the heart and lungs into the aorta artery, as I have explained in my 'Quaestiones Peripateticae.'[19,20]

William Harvey (1578 to 1657) of Folkestone, Kent, received his Doctor of Physic in 1602 from the foremost medical school of the day, the University of Padua. He received his Doctor of Medicine degree from the University of Cambridge that same year and began practice in London. From Harvey's first Lumleian Lectures to the College of Physicians in Surgery and Anatomy, manuscript notes reveal that Harvey had already formulated by 1616 his theory on the circulation:

> It is plain from the structure of the heart that the blood is passed continuously through the lungs to the aorta as by the two clacks of a water bellows to raise water.
>
> It is shown by the application of a ligature that the passage of the blood is from the arteries into the veins.
>
> Whence it follows that the movement of the blood is constantly in a circle, and is brought about by the beat of the heart. It is a question, therefore, whether this is for the sake of nourishment or rather for the preservation of the blood and the limbs by the communication of the heat, the blood cooled by warming the limbs being in turn warmed by the heart.[57]

International acclaim followed his formal publication of *De Motu Cordis* in 1628.

Stethoscopy

Exactly 200 years after Harvey's initial Lumleian Lecture, a French physician:

> walking in the court of the Louvre . . . saw some children, who, with their ears glued to the two ends of some long pieces of wood which transmitted the sound of the little blows of the pins, struck at the opposite end. . . . He conceived instantly the thought of applying this to the study of diseases of the heart. On the morrow, at his clinic at the Necker Hospital, he took a sheet of paper, rolled it up, tied it with a string, making a central canal which he then placed on a diseased heart. This was the first stethoscope.[73]

The Frenchman, of course, was Rene-Theophile-Hyacinthe Laennec (1781 to 1826). Laennec recalled fondly that:

> In 1816, I was consulted by a young woman labouring under general symptoms of diseased heart, and in whose case percussion and application of the hand were of little avail on account of the great degree of fatness. . . . I rolled a quire of paper into a sort of cylinder and applied one end of it to the region of the heart and the other to my ear, and was not a little surprised and pleased, to find that I could thereby perceive the action of the heart in a manner much more clear and distinct that I had ever been able to do by the immediate application of the ear. From this moment I imagined that the circumstance might furnish means of enabling us to ascertain the character, not only of the action of the heart, but of every species of sound produced by motion of all the thoracic viscera.[63,103]

A myriad of modifications were made on Laennec's stethoscope. Pierre-Adolphe Piorry (1794 to 1879) of Poitiers designed a more slender stem and attached a pleximeter in 1826.[80] This was followed 3 years later at Edinburgh Royal Infirmary by Nicholas P. Comins' invention of the first flexible stethoscope.[22] The physician who first completely described the murmurs of mitral stenosis,[101] Charles J. B. Williams (1805 to 1889) of London created a lead-tubed binaural stethoscope in 1843.[102] Dr. Arthur Leared of London gave the first public exhibition of a binaural stethoscope at the 1851 World Fair.[66]

That same year, Dr. Nathan B. Marsh received his US patent for stethoscopes having a "double branch connected with the main trunk, so as to enable persons to use both ears simultaneously."[75] A distant forerunner of the phonendoscope,[77] Marsh's stethoscope was inconvenient. One critic observed:

> Over the pectoral end of the instrument was stretched a membrane; two elastic tubes led from this to the ear. It is said that the ear pieces were inconvenient, and to use the instrument required both hands. It gave a muffled but loud sound caused by reverberation inside the instrument, due to the presence of the drum and the unequal bore."[77]

Better control of reverberation was achieved by Aurelio Bianchi of Florence, who devised the phonendoscope in 1894. Bianchi published details of this new instrument with Eugenio Bazzi the following year.[8] "The phonendoscope as it later appeared consisted of a heavy metallic cup with low margins, in which a light elastic hard-rubber diaphragm was made to vibrate both by sound waves and body movements. The instrument was made somewhat on the principle of the telephone. . . . Two long rubber tubes with earpieces connect[ed] with the cavity of the instrument."[77] A final modification in 1896 by Dr. H. B. Baruch of New York City affixed stethoscopic ear pieces to the ends of the rubber tubes of the phonendoscope.[4]

A year in the wake of the Baruch-Bianchi phonendoscope, in December of 1897, Robert C. M. Bowles of Brookline, Massachusetts, filed for design and utility patents on the Bowles stethoscope.[13] Not until 1901 did Bowles receive the latter US patent for:

> a stethoscopic instrument provided with an exposed diaphragm adapted to make contact with the body of a person, and with a back having a concaved front face . . . to form an air-chamber, and a substantially small curved sound delivery tube or pipe of substantially non-compressible material attached to said back near its center and extended toward the outer edge . . . to afford a smooth and unobstructed outlet for the sound-vibrations.[14]

Widely quoted in a report on the Bowles stethoscope in the *Johns Hopkins Bulletin*, Dr. Richard Clarke Cabot (1868 to 1939) characterized the Bowles stethoscope as "a simple diaphragm like that of the telephone, connected with the chamber into which the tube of the stethoscope enters. With it one can hear sounds deeper in the chest than those heard with any other stethoscope. . . . One can hear as much of the heart sounds through the clothes with this instrument as with any other instrument next to the skin."[2] As a leading Boston physician, Cabot helped lead a discussion of Harvey Cushing's "blood pressure observations"[26] at the program entitled "Consideration of Blood Pressure" held January 19, 1903.[56] As both an authority in auscultation and a leading proponent of the recently marketed Bowles stethoscope, Cabot acquainted Cushing with Bowles' instrument. Cabot's enthusiasm about "the Bowles" was not lost on Harvey Cushing during the conference in Boston.

Cushing returned to Baltimore, and within 28 months construction was completed on his Hunterian Laboratory for Experimental Medicine.[56] Named after anatomist John Hunter, the "old Hunterian" was America's first experimental surgical laboratory and also the veterinary hospital for Baltimore. However, the Hunterian's name "mystified Baltimoreans who thought the term had reference to pointers, retrievers, and setters."[56]

First on dogs in the Hunterian[27] and then on patients at Johns Hopkins Hospital, Harvey Cushing employed his personal Bowles stethoscope (Fig. 2.) in 1907 as the first intraoperative precordial monitor. His Bowles stethoscope was rather bulky at 2 inches in diameter and was used predominantly as a respiratory monitor during induction of general anesthesia. Particularly on the dogs, the Bowles would often need to be removed as the chest was opened. Removing the

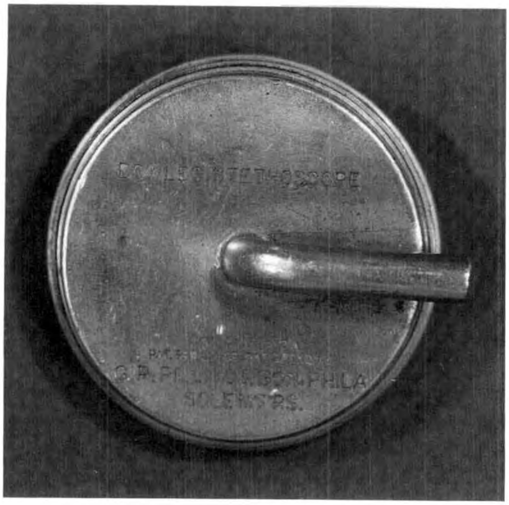


Figure 2. Harvey Cushing's personal Bowles stethoscope, the first precordial stethoscope.

monitor after induction (that is, during maintenance of anesthesia) was unsatisfactory, because both Cushing and surgeon-anesthetist S. Griffith Davis were anxious to avoid the "dread stage of respiratory paralysis . . . [and promote] quiet [respiration], with perhaps a very slight snore."[29] The binaural component of the Bowles stethoscope was not especially helpful in the operating room, because the anesthesiologist needed one ear free for communications from operating room personnel. In fact, within a year, the Bowles would be relegated to detecting Korotkoff sounds under Riva-Rocci's cuff.[61]

Over the next 12 months, Davis and Cushing sought to bring "a simple device . . . into general use—namely, the *continuous auscultation of cardiac and respiratory rhythm during the entire course of anesthesia*."[28] This monitoring device would have to be useful in the prone and other awkward positionings of the neurosurgical patient. Cushing wrote:

> With a patient in this prone position it is difficult for the anesthetist to gauge fully the variations in cardiac action, and during the past six months Dr. Davis has employed in these, as in all other operations, [a very simple device].
>
> The idea arose from a practice in the Hunterian Laboratory of auscultating the heart during the production of experimental valvular lesions, and like other things has been carried from laboratory to clinic. The transmitter of a phonendoscope is secured by adhesive strips over the precordium and connects by a long tube with the anesthetist's ear, where the receiver is held by a device similar to a telephone operator's headgear.
>
> Uninterrupted information of the patient's condition is thus given, and the anesthetist need not disengage a hand for the occasional palpation of the pulse, which is all that he is usually expected to do. On several occasions, by the prompt appreciation of change in the heart-beat or respiration thus acquired, it has been possible to avert what otherwise might have been surgical disasters.[28]

Future monitors would avert intraoperative disasters by assessing changes in blood circulation by means of continuous modalities like sonic accumulation, phonocardiography, and esophageal stethoscopy and echocardiography. Cushing's intraoperative auscultation with the Bowles stethoscope and Davis' more practical precordial monitoring with the phonendoscope were harbingers of sound (and ultrasound!) monitoring practices to come.

PULSATION

The pulse is the rhythm of life. The radial pulse has predominated as a diagnostic site for cardiovascular monitoring.

Egyptian: The Heart Speaks

As early as the "Old Kingdom" or "Pyramid Age" of the 30th to 26th centuries BC, the Egyptians valued the pulse as a measure or monitor of health in the present life.[1] Hieroglyphic phrases like "heart activity" and "the heart speaks" suggest the action of the pulse, and "counting" and "measuring" point to the likelihood that Egyptians counted pulse rate (Fig. 3). The 17th century BC saw the transcription of the first surgical textbook, the Edwin Smith Papyrus. This papyrus

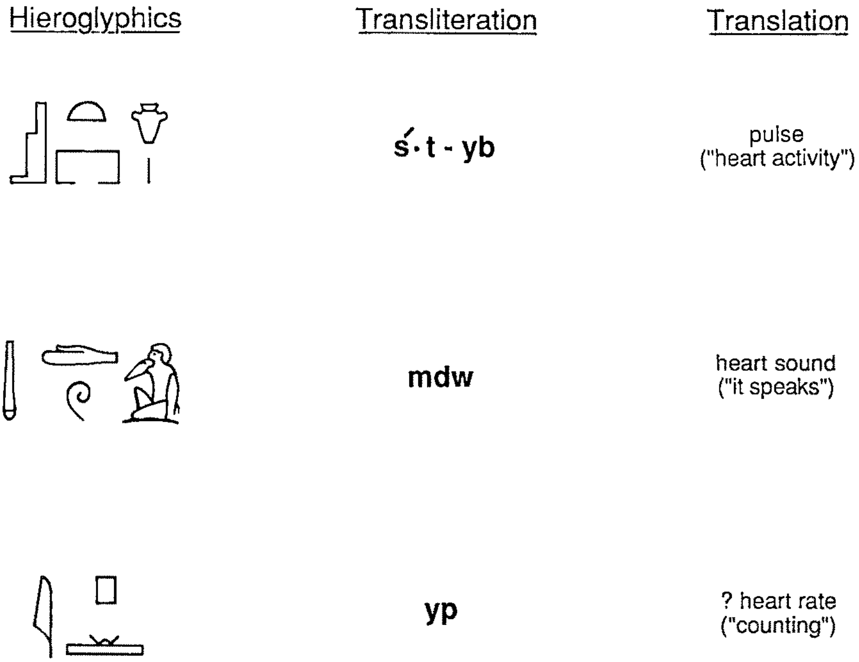


Figure 3. Referring to the heart and the pulse, these Egyptian hieroglyphics were gleaned from *The Secret Book of the Physician.*

gave instructions on cardiovascularly assessing the neurologically injured patient:

> 'Thou examinest a man,' [it means] counting any one——[like cou]nting things with a bushel. (For) examining (measuring) is [like] one's [counting] a certain quantity with a bushel, (or) counting something with the fingers, in order to [know]———. It is measuring things with a bushel which———one in whom an ailment is [cou]nted, like measuring the ailment of a man; [in order to know the action] of the heart. There are canals (or vessels) in it (the heart) to [every] member. Now if the priests of Sekhmet or any physician put his hands (or) his fingers [upon the head, upon the the back of the] head, upon the two hands, upon the pulse, upon the two feet, [he] measures [to] the heart, because its vessels are in the back of the head and in the pulse; and because [its pulsation is in] every vessel of every member. He says 'measure' regarding his [wound] because of the vessels to his head and to the back of his head and to his two feet———his heart in order to recognize the indications which have arisen therein; meaning [to meas]ure it in order to know what is befalling therein.[15]

Chinese: The 12 Pulses

The ancient Chinese elevated the taking of the pulse to an art. According to the *Nei Ching,* very early in the morning was the best time of day for taking the pulse "when the breath of Yin has not yet begun to stir and when the breath of Yang has not yet begun to diffuse. . . ."[92] Generally, only the radial pulses were examined. The pulse diagnostician would examine a male patient's left radial pulses prior to the right ones and a female's right ones before her left. Each hand's radial pulsation was divided into inch, bar and cubit regions, each of which could be palpated deeply (the internal or Yin pulse) or superficially (the external or yang pulse).[104] Thus a total of 12 pulses, six on each hand, required monitoring (Fig. 4). Note that the *Nei Ching* and the European acupuncturists agree on the meridians or organ systems represented by the six deep or yin pulses; however, these sources disagree on the organs represented by the superficial pulses (Fig. 4).

Acupuncture and moxibustion were developed as treatment modalities for ministering to imbalances perceived in the 12 organ systems or meridians. Modern European and Chinese acupuncture reflects the evolution of Chinese pulse diagnosis after the dissemination of *Mei Ching* ("*The Classic of the Pulse*"), a ten-volume reference written by Wang Shu Ho (265 to 317 BC).[41]

Indian: The Ayurvedic Tridoshas

In order to be in Tridhatus or a state of balance, the three life forces Vayu, Kapha, and Pitha must be in perfect balance. When they are imbalanced, these are referred to as the three faults or Tridoshas. To monitor a patient's health, the physician merely needs to palpate the radial pulse, the "Witness to the Soul."

Pulse anthologists Amber and Babey-Brooke summarize Ayurvedic pulse monitoring as follows:

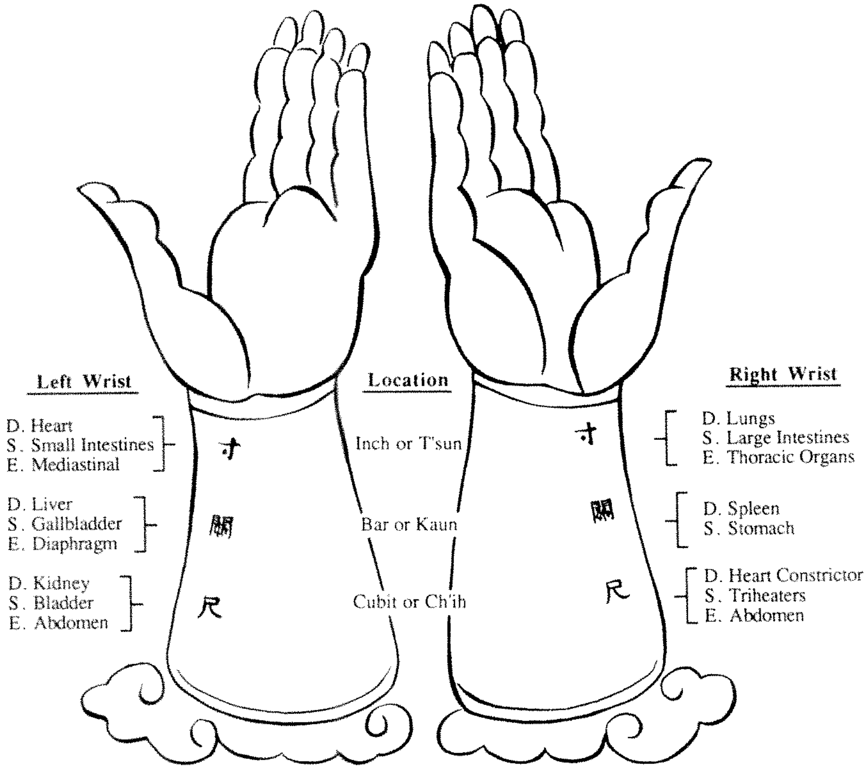


Figure 4. The 12 Chinese pulses included 6 yang or deep (D.) pulses and 6 yin or superficial ones. The original meridians represented by the superficial pulses have evolved from those of the *Nei Ching* (S.) to those of the modern European acupuncturists (E.).

> First, the pulse at the wrist or the radial pulse is the one that is usually preferred and is examined with three fingers.
>
> The male patient extends his right hand for his pulse to be taken, but the female extends her left hand. This practice is reversed in the Chinese technique.
>
> The examiner uses the three fingers of his right hand: the index, the middle, and the ring finger or otherwise described as the second, third, and fourth fingers, and he places these three in a position two fingers in width below the root of the thumb. The physician uses his left hand to press the artery of the elbow and holds the patient's hand in a slanting manner while he places his right hand in the manner described above. . . . A heavy pulse to the index finger shows air; to the middle finger shows fire; and to the ring finger shows water. . . . The pulse becomes fast with air, jumpy with fire, and slow with water.[1]

Greek: Observation of Pulse

Praxagoras' disciple, Herophilus (f. 315 BC) of Chalcedon used a clepsydra, an Egyptian water clock, to measure pulse rate in Alexandria. He also delineated four cardinal properties of the pulse: frequency, rhythm, size, and strength. With his phrase "*pulsus caprizans*," Herophilus likened the forcible pulse following an extrasystole to the leaping of a goat. Nearly 2,000 years would pass before man would again monitor the pulse as accurately as Herophilus had done.

Venous Access and Pulsations

Forsaking Herophilus' goat, Sir Christopher Wren experimented on dogs in 1656. Combining opium, wine, and ale inside a pig's bladder, Sir Christopher Wren infused the mixture through a goose quill into a dog's vein. Venous access was born!

Fifty years later, public anxiety over a rash of sudden deaths in Rome prompted still further investigations of the venous system, its distention, and its pulsations. The following year, in 1707, Giovanni Maria Lancisi (1654 to 1720) published his observations on the association of cardiomegaly with sudden death.[64] The brilliant Lancisi differentiated between cardiac dilatation and hypertrophy. By 1728 he had correlated jugular venous distention with right heart dilatation.[65] Lancisi's careful examination of the jugular venous pulsation and distention formed the basis for his discussion of tricuspid regurgitation.

Direct Measurement of Pulsation

Geddes has classified major early investigations of direct blood pressure measurement into mechanical, mechano-optical, electrolytic, and strain-gauge manometry.[50]

The Rector of Farringdon, Hampshire, and Minister of Teddington, Middlesex, Reverend Stephen Hales began informal blood pressure investigations on the crural (femoral) arteries of dogs in 1708. Hales reported that "about six years afterwards I repeated the like Experiments on two horses, and a fallow Doe." In his 1733 publication *Statical Essays*, Hales renders "An *Account* of some Hydraulick and Hydrostatical *Experiments* made on the Blood and Blood-Vessels of *Animals*" with the following as "Experiment I":

> In *December* I caused a Mare to be tied down alive on her Back, she was fourteen Hands high (56 inches), and about fourteen Years of Age, had a *fistula* on her Withers (shoulders), was neither very lean, nor yet lusty: Having laid open the crural Artery about three Inches from her Belly, I inserted into it a brass Pipe whose Bore was one sixth of an Inch in Diameter; and to that, by means of another brass Pipe which was fitly adapted to it, I fixed a glass Tube, of nearly the same Diameter, which was nine Feet in Length: Then untying the Ligature on the Artery, the Blood rose in the Tube eight Feet three Inches perpendicular above the Level of the left Ventricle of the Heart: But it did not attain to its full Height at once; it rushed up about half way in an Instant, and afterwards gradually at each Pulse twelve, eight, six, four, two and sometimes one Inch: When it was at its full Height, it would rise and fall at and after each Pulse two, three, or four Inches; and sometimes it would fall twelve or fourteen Inches, and have there for a time the same

Vibrations up and down at and after each Pulse, as it had, when it was at its full Height; to which it would rise again, after forty or fifty Pulses.[55]

Unwieldy as this long manometer was, Hales' achievement was a landmark in cardiovascular monitoring (Fig. 5).

As part of his 1828 graduation dissertation, medical student Jean-Leonard-Marie Poiseuille (1799 to 1869), characterized his "hemodynamometer," a compact, mercury-filled U-tube manometer whose hollow lead end contained potassium carbonate as an anticoagulant. While measuring canine blood pressure with his hemodynamometer, Poiseuille demonstrated variation of blood pressure with respiration. It was Poiseuille's work that popularized mm Hg as units for measuring blood pressure.[81]

In order to disprove theories of a right-to-left heart temperature difference, Claude Bernard resurrected Hale's long rod approach to vascular access in 1844. However, Bernard employed a long mercury

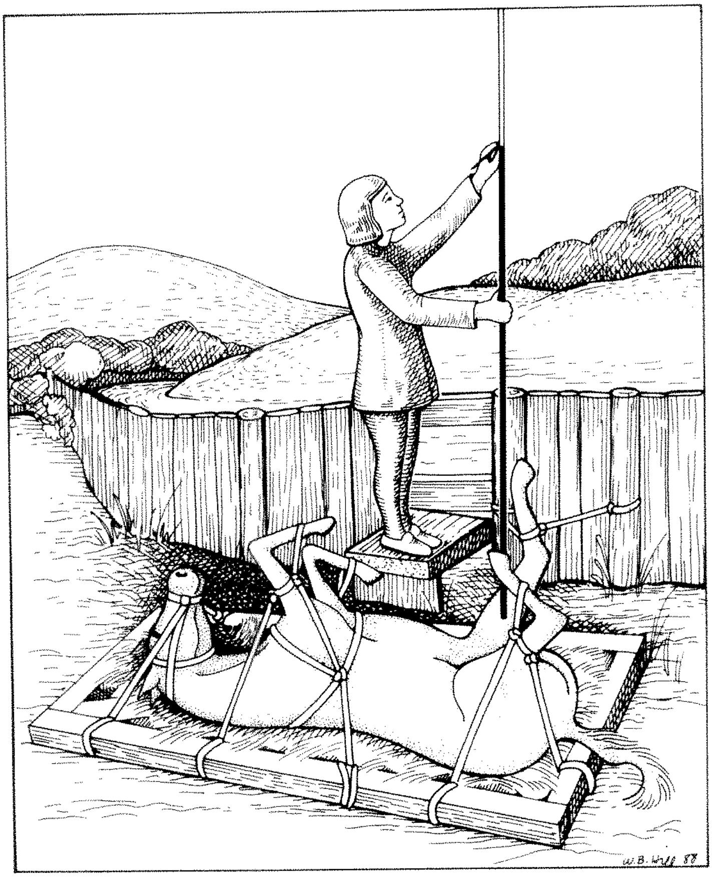


Figure 5. Experiment I from Reverend Hales' *Statical Essays:* the first direct measurement of blood pressure.

thermometer to cannulate first the equine carotid artery and left ventricle and then the internal jugular vein and right ventricle. At the horse's autopsy, Bernard learned that he had caused pericardial tamponade secondary to right ventricular perforation.[6] Thus Bernard was the first to demonstrate a major complication from central venous monitoring.[79]

A professor of anatomy, anatomy and physiology, and physiology at, respectively, Marburg, Zurich, and then Leipzig, Carl F. W. Ludwig (1816 to 1895) pioneered the graphic method of investigation in 1847. Sketching his new method of using the recording mercury manometer with a smoked drum kymograph, Ludwig wrote that "In order to secure a good value from Poiseuille's mercury manometer, and in order to get the time relations of the changes in pressure, put a staff-like float on the mercury at the upper end of which is a pointer. Let the fluctuations be written on a surface which passes by the pointer with uniform speed. In this way one secures curves, the height of which is an expression of the blood pressure and the duration of which is an expression of time."[69]

Clinical and laboratory research continued with the manometer. During a surgical procedure in 1856, Faivre connected a patient's femoral artery to a mercury manometer and found a direct arterial pressure of 120 mm Hg.[37] By 1878 Golz and Gaule had added a double check valve to the manometer in order to obtain maximum and minimum blood pressure.[52]

A different mechanical system for measuring pressures involved air transmissions through a double-lumen tube. Following work near Paris at the School of Veterinary Medicine at Alfort, Etienne-Jules Marey (1830 to 1904) and Chaveau crafted in 1861 this more rapidly responding pneumatic system. They observed, "One can be reassured of the innocuity of this method by examining the horse, who is scarcely disturbed, walks and eats as usual. In only a few instances is the pulse rate slightly increased, especially at the time of the catheter's introduction within the heart cavities."[21] These two investigators have been credited with reporting the first dysrhythmic complications of central venous access.[79] Note that neither scientist extended this catheterization to man.

Fick published details in 1864 of yet another mechanical system, his C-spring recorder for blood pressure measurement,[38] almost 15 years after its basic principle had been elucidated. Back in 1849, a railway engineer, R. E. Schinz of Switzerland had designed a C-shaped, thin-walled, hollow metal tube which uncoiled as a gauge of increasing pressure.[88] Bourdon popularized the gauge of Schinz at the Academy of Science in 1853, and thereafter this coiled pressure gauge was known as the Bourdon gauge.[11] The Bourdon gauge is still employed today to register pressure from compressed gas cylinders. The biphasic wave resulting from Fick's C-spring was disappointing, especially in light of Landois' work. In 1872 Landois demonstrated that a moving paper surface could be sprayed by the stream of blood pulsing from a fine needle that Landois placed in the tibial artery of a large dog. Recording not only systolic and diastolic pressures, Landois' hemautogram demonstrated the existence of the dicrotic notch.[68] Four years after Landois' hemautogram, Fick built a straight-spring recorder for measuring blood pressure.[39]

A tremendous advance came in 1906, when Sir James Mackenzie (1853 to 1925) created the ink polygraph with the technical help of a watchmaker.[71] Mackenzie recalled:

> In my early days when investigating the action of the heart, I attached a tambour to the upright stem of a Dudgeon sphygmograph in such a manner that I was able to obtain, at the same time as the radial pulse was being recorded, some other movement, as the jugular pulse, apex beat, or carotid. As, however, there was a good deal of inconvenience in the blackening and varnishing the papers, and as it was not possible to get a long tracing upon the heart's rhythm, I discarded this for the ink polygraph.[103]

Progress was also being made in the field of human central vascular catheterization. Following his research on cirrhosis,[9] Bleichroeder reported having passed ureteral catheters into arteries and veins of both dogs and humans as early as 1905. He obtained inferior vena caval blood specimens near the hepatic vein for his cirrhosis research. Nonetheless, he "did not believe the experiments to be of any practical value and left them unpublished."[79] Bleichroeder's catheterization experiments[10] appear to have preceded the published reports of Werner Forssmann who catheterized his own right heart with a 4 French ureteral catheter in 1929.[42]

Meanwhile, a host of new technologies emerged. Mechano-optical systems were investigated first by Otto Frank[43–45] and then by Wiggers.[99,100] Electrolytic manometry was explored by Grunbaum in 1897[53] and eventually by Garten in 1916.[49] As early as 1876, Tomlinson had published that stretching a wire produced a change in its electrical resistance.[91] This basic principle behind strain-gauge manometry remained available but unutilized for 66 years. Geddes has thoroughly and thoughtfully reviewed the complicated evolution of direct gauges of blood pressure.[50]

By the end of the Great War, man had successfully cannulated arteries and central veins. Man had also begun to appreciate pulsations on both sides of the heart. A grand frontier of discovery lay ahead and still lies ahead for invasive waveform monitoring.

Indirect Measurement of Pulsation

Having briefly examined direct gauges of pulsation, step back now to explore the more clinically applicable world of indirect gauges of pulse. Indirect measurement of blood pressure evolved from solid- to liquid- to gas-filled devices and eventually vacillated back and forth between liquid and gas. A professor of physiology at the University of Tubingen, Karl Vierordt (1818 to 1884) determined in 1855 the counterweight required to obliterate the human radial pulse.[93] Not until

P24644

1876 was the first practical arterial occluder, a water-filled bag or pelotte, devised by Ritter Samuel Siegfried K. von Basch of Germany (1837 to 1905).[95] Von Basch studied only systolic pressure. Pierre-Carl-Edouard Potain of Paris (1825 to 1901) employed an air-filled pelotte.[82] By 1876 Etienne-Jules Marey of Paris (1830 to 1904) had reverted back to hydraulic counterpressure on the forearm.[74] In a final victory for pneumatics, Scipione Riva-Rocci designed his sphygmomanometer in 1896 at the University of Pavia in Italy. The Riva-Rocci apparatus employed an air-inflated, arm-occluding cuff that was only 5 cm wide.[84]

That same year, 1896, Harvey Williams Cushing began his surgical residency at Johns Hopkins Hospital. After completing, "in the house," his 4 years under Halsted, Cushing travelled throughout Europe during 1900 and 1901 to gain experience in clinical and experimental neurosurgery. While iceskating and mountain climbing for recreation during his Swiss winter with Kocher in Berne, Cushing developed a cough that nagged him through the spring. Hoping a warmer climate would improve his health, a reluctant Cushing boarded a train for Italy.[30,47]

Mankind was blessed indirectly by that nagging cough. After arriving in Pavia, Italy, Cushing recorded the following entry in his 1901 diary:

> *Pavia* May 6 . . . Ospidale di St. Matteo. Just back of the University. Riva-Rocci at his [Osstaldi] in Vargese. Rarely comes to hospital. Dali Edmondo *Orlandi* at present is first assistant. Very kind. Speaks German. Also next door Giovanni Grassi. Saw an O.P.D. Clinic in A.M. with a row of cherubic Pavia girls with their fore arms bared having injections of iron. Blood pressure apparatus at all hands. Many of them in each ward. Orlandi has made a very simple one. Riva-Rocci's apparatus is *home made.*[24]

An excellent artist, Cushing sketched Riva-Rocci's "sfigmomanometro" in his diary for future reference (Fig. 6). Upon returning to Baltimore in September 1901, Cushing began insisting that blood pressures be measured and recorded intraoperatively.[25] That same month witnessed Cushing's addition of blood pressure to the pulse/respiration anesthetic record that Amory Codman and he had pioneered while medical students at Harvard.[5,59,90]

Thus by the close of 1901, Cushing had transported the Riva-Rocci sphygmomanometer from Italy, Einthoven had reported his string galvanometer, and Bowles had received a patent for his stethoscope. The stage was now set for adding continuous modalities like precordial and electrocardiographic monitoring to Cushing's modern anesthetic record.

The history of cardiovascular monitoring has walked hand in hand with man's need through the centuries to assess patients with head injuries. Who but the neurotraumatized patient can bear such mute testimony to cardiovascular instability? It was no accident that ancient Egypt's *Secret Book of the Physician* was gleaned from the neurosurgical section of the Edwin Smith Papyrus almost 37 centuries

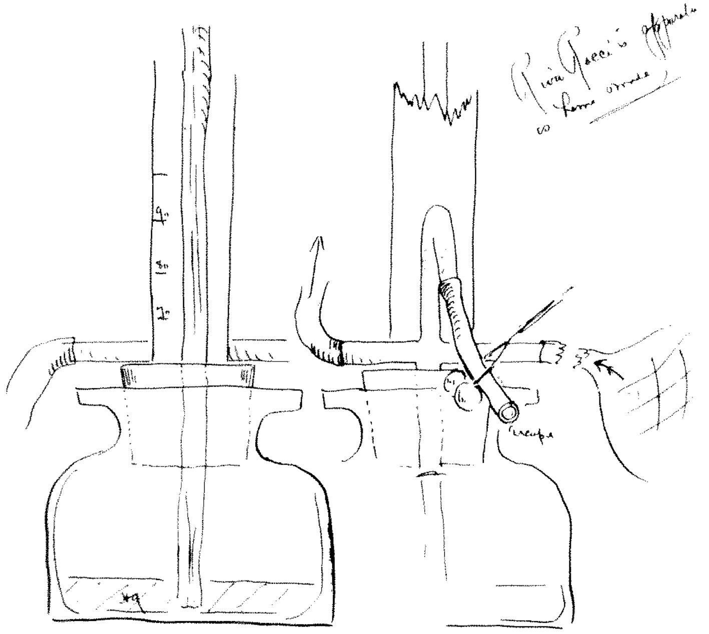


Figure 6. Harvey Cushing's rough sketch of Riva-Rocci's "sfigmomanometro." (Courtesy of Yale University.)

ago. Nor was it accidental that the first physician to incorporate precordial and sphygmomanometric monitoring into anesthetic practice was none other than the consummate neurosurgeon, Harvey Williams Cushing.

ACKNOWLEDGMENT

I am indebted to Ferenc Gyorgyey and Susan Alon of the Yale Medical History Library for their valuable advice. I am grateful for the medical illustrations executed by Wendolyn B. Hill, Carol Porter, and Virginia Simon.

REFERENCES

1. Amber RB, Babey-Brooke AM: The Pulse in Occident and Orient: Its Philosophy and Practice in India, China, Iran, and the West. New York, Dunshaw Press, 1966
2. Anonymous: Surgical and Orthopaedic Apparatus, Invalids Articles, Circular 77. Boston, Codman & Shurtleff, undated
3. Arcieri JP: The Circulation of the Blood and Andrea Cesalpino of Arezzo. New York, SF Vanni, 1945, p 193
4. Baruch HB: Med Record (New York) 50:624, 1896
5. Beecher HK: The first anesthesia records (Codman, Cushing). Surg Gynecol Obstet 71:689–693, 1940
6. Bernard C: Leçons sur la Chaleur Animale. Paris, Librairie J.-B. Bailliere et Fils, 1876, pp 42–81

7. Bernstein J: Uber den zeitlichen Verlauf der negativen Schwankung des Nervenstroms. Pflugers Arch 1:173, 1868
8. Bianchi A, Bazzi E: Clinica Moderna (Florence) I:421, 1895
9. Bleichroeder F: Virchow Arch Pathol 177:435, 1904
10. Bleichroeder F: Berl Klin Wochenschr 49:1503, 1912
11. Bourdon E: Note sur les tubes à section transversale non circulaire. Compt Rend Acad Sci 37:636–637, 1853
12. Bousfield G: Angina pectoris. Lancet 2:457, 1918
13. Bowles RCM: Stethoscopic instrument, U.S. Design Patent No. 28,307. *In* Official Gazette of U.S. Patent Office 82:1201, 1898
14. Bowles RCM: Stethoscope, U.S. Patent No. 677,172. *In* Official Gazette of U.S. Patent Office 95:2604, 1901
15. Breasted JH: The Edwin Smith Surgical Papyrus, vol. I. Chicago, University of Chicago Press, 1930, pp 102–114
16. Burch GE, DePasquale NP: A History of Electrocardiography. Chicago, Year Book Medical, 1964
17. Burnett J: The origins of the electrocardiograph as a clinical instrument. Med History S5:53–76, 1985
18. Castiglioni A: A History of Medicine, ed 2. Translated by E. B. Krumbhaar. New York, Alfred A. Knopf, 1947
19. Cesalpino A: Quaestionum Peripateticarum. Venice, 1571, p 125
20. Cesalpino A: Quaestionum Medicarum, vol. 2, ed 2. Venice, 1593, p 234
21. Chauveau A, Marey E-J: Appareils et Experiences Cardiographiques Demonstration Nouvelle du Mecanisme des Mouvements du Coeur par l'emploi des Instruments Enregistreurs à Indications Continues. Mem Acad Mede 26:268, 1863
22. Comins NP: Lancet ii:685, 1828–1829
23. Cumston CG: The biography of Michel Servetus, the discoverer of the pulmonary circulation: to which is appended the text of that passage of his work relating to that discovery, followed by an English translation of the same and notes. Boston Med Sci J 156:451–461, 1907
24. Cushing HW: European Notes: 1900–1901, vol. 3. New Haven, Yale Medical History Library, diary entry for May 6, 1901
25. Cushing HW: On the avoidance of shock in major amputation by cocainization of large nerve trunks preliminary to their division. With observations on blood pressure changes in surgical cases. Ann Surg 36:321–345, 1902
26. Cushing HW: On routine determinations of arterial tension in operating room and clinic. Boston Med Surg J 148:250–256, 1903
27. Cushing HW: Experimental and clinical notes on chronic valvular lesions in the dog and their possible relation to a future surgery of the cardiac valves. J Med Res 12:471–486, 1908
28. Cushing HW: Some principles of cerebral surgery. JAMA 52:184–192, 1909
29. Davis SG: The administration of ether by the drop method. Md Med J (May) 1907
30. Denzel JF: Genius with a Scalpel: Harvey Cushing. New York, Julian Messner, 1971
31. DuBois-Reymond E: Vorlaufiger Abriss einer Untersuchung uber den sogennanten Froschstrom und uber die elektromotorischen Fische. Ann Phys Chem 58:1, 1843
32. DuBois-Reymond E: Aire et sur la modification qu'eprouve cette loi par l'effet de la contraction. Ann Chim Phys 30:119, 1850
33. Ebbell B: The Papyrus Ebers: The Greatest Egyptian Medical Document. Copenhagen, Levin and Munksgaard, 1937
34. Einthoven W: Un nouveau galvanometre. Arch néerl Sci exactes nat 6:625, 1901
35. Einthoven W: Die galvanometrische Registrirung des Menschlichen elektrokardiogramms, Zugleich eine Beurtheilung der Amvendung des Cupillar elektrometers in der Physiologie. Pflugers Arch 99:472, 1903
36. Elgood C: Medicine in Persia. *In* Krumbhaar EB (ed): Clio Medica, A Series of Primers on the History of Medicine. New York, Paul B. Hoeber, 1934

37. Faivre J: Etudes experimentales sur les lesions organiques du coeur. Gaz Med Paris, 1856, p 727
38. Fick A: Ein neuer Blutwellenzeichner. Reicherts u du Bois-Reymond's. Arch Anat Physiol S583:543–548, 1864
39. Fick A: Ein verbesserung des Blutwellenzeichners. Arch Physiol 30 S592:608–612, 1883
40. Flint HL: The Heart: Old and New Views. New York, Paul B. Hoeber, 1921
41. Forke A: Mo Ti des Sozialethikers und seiner Schuler philosophische Werke. Mitteilungen d Seminar f Orientalische Sprachen, vol 23–25. Berlin, Bei Bande, 1922
42. Forssmann W: Die Sondierung des Rechten Herzens. Klin Wochenschr 8:2085, 1929
43. Frank O: Kritik der elastischen Manometer. Z Biol 44:445–613, 1903
44. Frank O: Die Theorie der Segmentkolbenkapsel. Zschr Biol 59:526–530, 1912–1913
45. Frank O: Ein neues optisches Federmanometer. Zschr Biol 82:49–65, 1924
46. Fulton JF: Selected Readings in the History of Physiology. Springfield, IL, Charles C Thomas, 1930
47. Fulton JF: Harvey Cushing—A Biography. Springfield, IL, Charles C Thomas, 1946
48. Galvani LA: De viribus electricitatis in motu musculari commentarius. Comment Bonon Scient et Art Inst Bologna 7:363, 1791
49. Garten S: Beitrage zur Lehre vom Kreislauf. Zschr Biol 66:23–82, 1916
50. Geddes LA: The Direct and Indirect Measurement of Blood Pressure. Chicago, Year Book Medical, 1970, pp 9–36
51. Ghalioungui P: Magic and Medical Science in Ancient Egypt. London, Hodder and Stoughton, 1963
52. Golz F, Gaule J: Uber die Druckverhaltnisse im Innern des Herzens. Arch Physiol Menschen Thiere Bonn 18:100–135, 1878
53. Grunbaum OF: On a new method of recording alterations of pressure. J Physiol 22:xlix–li, 1897–1898
54. Haddad SI, Khairallah AA: A forgotten chapter in the history of the circulation of the blood. Ann Surg 104:1–8, 1936
55. Hales S: Statical Essays: Containing Haemastaticks; or, an Account of Some Hydrostatical Experiments Made on the Blood and Blood-Vessels of Animals, vol. II. London, W. Innys & R. Manby, 1733
56. Harvey AM: Harvey Williams Cushing: The Baltimore Period, 1896–1912. Johns Hopkins Med J 138:196, 1976
57. Harvey W: First Lumleian Lectures by William Harvey (manuscript notes). British Museum, April 16–18, 1616
58. Heard JD, Straus AE: A report on the electrocardiographic study of two cases of nodal rhythm exhibiting R-P intervals. Am J Med Sci 155:238–252, 1918
59. Hirsch NP, Smith GB: Harvey Cushing: His contribution to anesthesia. Anesth Analg 65:288–293, 1986
60. Jolly WA, Ritchie WT: Auricular flutter and fibrillation. Heart 2:177, 1911
61. Korotkoff NS: On the subject of methods of measuring blood pressure. Bull Imp Military Med Acad St. Petersburg 11:365–367, 1905
62. Krumbhaar EB: Electrocardiographic observations in toxic goiter. Am J Med Sci 155:175–203, 1918
63. Laennec RTH: A Treatise on the Diseases of the Chest, in Which They Are Described According to Their Anatomical Characters, and Their Diagnosis Established on a New Principle by Means of Acoustick Instruments. (Translated by John Forbes) First American ed. Philadelphia, J. Webster, 1823, p 319
64. Lancisi GM: De Subtaneis Mortibus. Rome, 1707
65. Lancisi GM: De Motu Cordis et Aneurysmatibus. Naples, 1728
66. Leared A: NY Med Times IV:140, 1855
67. Lockhart ML: Electrostethograph, U.S. Patent No. 2,099,938. *In* Official Gazette of U.S. Patent Office 484:845, 1937

68. Luciani L: Human Physiology, translated by FA Welby, vol. 1. London, Macmillan & Co., Ltd., 1911, p 592
69. Ludwig C: Beitrage zur Kenntniss des Einflusses der Respirations bewegungen auf den Blutlauf im Aortensysteme. Muller's Arch Anat Physiol Wissensch Med, 1847, pp 240–302
70. Lyons AS, Petrucelli RJ: Medicine: An Illustrated History. New York, Harry N. Abrams, 1987
71. Mackenzie J: The ink polygraph. Br Med J i:1411, 1908
72. MacWilliam JA: Fibrillar contraction of the heart. J Physiol 8:296, 1887
73. Major RH: A History of Medicine, vol. 2. Springfield, IL, Charles C Thomas, 1954
74. Marey EJ: Pression et vitesse du sang. *In* Physiologie Experimentale. Travaux du Laboratoire de M. Marey. Paris, Masson & Cie, 1876, pp 236–371
75. Marsh NB: Improvement in stethoscopes, U.S. Patent No. 8,591. *In* Report of the Commissioner of the United States Patent Office, U.S. House of Reps. Doc. No. 102, Washington, 1851
76. Meyerhof M: Ibn an-Nafis (XIIIth cent.) and his theory of the lesser circulation. Isis 23:100–120, 1935
77. Morgan JD, Lamb DS: Laennec and the Stethoscope. Washington, DC, Heresford Press, 1910
78. Oersted JC: Experimenta circa effectum conflictus electrici in acum magneticam. J Chem Phys 29:275, 1820
79. Peters JL: Historical review. *In* A Manual of Central Venous Catheterization and Parenteral Nutrition. Littleton, MA, John Wright PSG Inc., 1983, pp 3–11
80. Piorry PA: De la percussion mediate. Paris, 1828
81. Poiseuille JLM: Recherches sur la force du coeur. Arch Gen Med, 1828, p 18
82. Potain PCE: La Pression Arterielle chez l'Homme a l'Etat Normal et Pathologique. Paris, Masson & Cie, 1902, p 191
83. Resnick R, Halliday D: Physics: Parts I and II Combined, Wiley International edition. New York, John Wiley & Sons, 1966, p 648
84. Riva-Rocci S: Un nuovo sfigmomanometro. Gaz Med Torino 47:981–1001, 1896
85. Rollason WN: Electrocardiography for the Anaesthetist. Oxford, Blackwell Scientific Publications, 1964
86. Said HM: Greco-Arab Concepts on Cardiovascular Diseases. Karachi, Pakistan, Hamdard Foundation Press, 1983
87. Samojloff A: Reminiscences of the late Professor Willem Einthoven. Am Heart J 5:545–548, 1930
88. Schinz RE: Das Schinz'sche Dampfmanometer fur Locomotiven. Dingler's Polytech J 113:85–90, 1849
89. Servetus M: De Restitutio Christianismi. Vienna, 1553, p 170
90. Shephard DAE: Harvey Cushing and anaesthesia. Can Anaes Soc J 12:832–842, 1965
91. Tomlinson H: On the increase in resistance to the passage of an electric current produced on stretching. Proc R Soc 25:451–453, 1876–7
92. Veith I: Huang Ti Nei Ching Su Wen: The Yellow Emperor's Classic of Internal Medicine. Berkeley, University of California Press, 1972
93. Vierordt K: Die Lehre vom Arterienpulses. Braunschweig, 1855, S. 21
94. Volta A: An account of some discoveries made by M. Galvani, with experiments and observations on them. Phil Trans R Soc, London, 1793
95. von Basch S: Ueber die Messung des Blutdrucks am Menschen. Z Klin Med 2:79, 1880
96. Waller AD: A demonstration on man of electromotive changes accompanying the heart's beat. J Physiol 8:229, 1887
97. Walsh J: Phil Trans Lond, 1773, pp 461–477
98. Walsh J: Correspondence to Benjamin Franklin, 1774
99. Wiggers CJ: Some factors controlling the shape of the pressure curve in the right ventricle. Am J Physiol 33:382–396, 1914
100. Wiggers CJ, Baker WR: A new universal optical manometer. J Lab Clin Med 10:54–56, 1924
101. Williams CJB: Diseases of the Chest, ed 3. London, Churchill, 1835

102. Williams CT: Laennec and the evolution of the stethoscope. Br Med J ii:6–8, 1907
103. Willius FA, Dry TJ: A History of the Heart and the Circulation. Philadelphia, W.B. Saunders Co., 1948
104. Wong KC: The pulse lore of Cathay. China Med J 42:884–897, 1928

Department of Anesthesiology
Yale University School of Medicine
333 Cedar Street
PO Box 3333
New Haven, CT 06510

0889–8537/88 $0.00 + .20

Preoperative Cardiovascular Monitoring

Martin J. London, MD, and*
Dennis T. Mangano, PhD, MD†

The choice of appropriate preoperative cardiovascular monitoring and diagnostic testing should be based on an adequate knowledge of the incidence and characteristics of perioperative cardiac mortality and morbidity. As well, the clinician should be familiar with the known risk factors for its occurrence. Although some of these concepts are summarized in this article, the reader is referred elsewhere for a more comprehensive review.[36] The following discussion deals with several commonly accepted, as well as some recent developments in, monitoring and diagnostic techniques. The emphasis is on those critically evaluated by clinical studies, especially in relation to patient outcome. The majority of the studies cited involve major noncardiac, especially vascular, surgery. The theoretical basis of each modality is presented, followed by a review of the relevant clinical studies.

ELECTROCARDIOGRAPHIC MONITORING TECHNIQUES: TWELVE-LEAD ECG, AMBULATORY ST-SEGMENT MONITORING, AND EXERCISE STRESS TESTING

Theoretical Basis

Electrocardiographic techniques allow the clinician to evaluate the patient from several different perspectives. The 12-lead resting ECG provides important information regarding acute or prior myocardial infarction, as well as other important morphologic characteristics (ventricular hypertrophy, conduction abnormalities, etc.). The exercise stress test, also usually performed using 12 leads, provides a relatively sensitive means to detect coronary artery disease (CAD). The type of ECG response provides important prognostic information.

University of California, San Francisco, University of California Medical Center and Veterans Administration Medical Center, San Francisco, California

*Assistant Professor of Anesthesia
†Professor of Anesthesia

Ambulatory ST-segment monitoring, currently limited to three leads, may provide important information on the frequency and nature of the ischemic pattern, even in the absence of symptoms. The latter technique, which has gained substantial popularity in recent years, is now being investigated in the perioperative setting.

Interpretation of ECG data is critically dependent on the prevalence of CAD in the population being studied.[6] Application of these techniques to younger age groups, females, and asymptomatic individuals is likely to yield a higher incidence of false-positive responses. In patients with or at high risk for CAD, accuracy increases substantially.[14] However, even in this group many factors may affect sensitivity and specificity,[14,24] including physiologic changes (electrolyte, temperature, respiratory, or other metabolic changes), medications (digoxin), and abnormal baseline ECG morphology (Q waves, resting ST-T abnormalities, ventricular hypertrophy, conduction abnormalities).

The sensitivity of Q-wave abnormalities on the resting 12-lead ECG for the presence of autopsy-verified myocardial infarction ranges from 33 to 62 per cent, while the specificity ranges from 88 to 98 per cent.[54] The presence of Q waves or ST-segment elevation correlates well with akinetic regions detected by contrast ventriculography, although coronary artery localization is not precise.[3,21] The number of Q waves correlates with the degree of ventricular dysfunction following myocardial infarction.[30] Other characteristics such as ST-T abnormalities, changes in R-wave voltage, QRS axis, and R/S ratio correlate poorly with wall motion.[3]

ST-segment depression of the appropriate magnitude during exercise (>1 mm horizontal or downsloping, 1.5 mm slowly upsloping) in a patient population with high disease prevalence is a sensitive marker of CAD, although coronary artery localization is poor.[14] Lead V_5 is the most sensitive lead for detecting ischemia during stress testing and ambulatory monitoring, as well as in the operating room.[12,37] The sensitivity of ST depression for the detection of CAD on exercise treadmill testing ranges from 56 to 81 per cent, while its specificity ranges from 72 to 96 per cent depending on the testing protocol. Its sensitivity increases with the number of diseased vessels (one vessel = 40 to 84 per cent, two vessels = 63 to 91 per cent, three vessels = 79 to 100 per cent).[12,14] The accuracy of a positive treadmill test is increased in older patients, patients with multiple clinical risk factors, exercise-induced angina, inadequate blood pressure response during exercise, or ST depression occurring in multiple leads.[12,14]

A number of recent studies have documented that patients with stable angina have frequent episodes of significant ST depression, often for prolonged periods, during daily life. The majority of these episodes occur in the absence of chest pain (75 per cent) and with normal heart rates.[18] Reduction of coronary blood flow during both symptomatic and asymptomatic ST depression has been demonstrated using rubidium positron tomography. The majority of ischemia in these patients is thought to be caused by cyclical changes in coronary vasomotor tone.[18,44] Patients with unstable angina are more likely to manifest ST elevation, indicative of severe transmural ischemia.[7,15] In contrast, ST elevation is very rare in patients with stable angina. During unstable angina, patients with concurrent silent ischemic episodes have a poorer prognosis than those without.[40] However, the prognostic significance of silent ischemic episodes in patients with stable angina alone is controversial.[40]

Clinical Studies

There are few well-designed prospective studies on the value of the routine preoperative ECG. In a retrospective study, Rabkin found that although new Q waves were detected in 2 to 3 per cent of patients over the age of 60 (over a mean interval of 25 months prior to surgery), no operations were delayed because of these findings.[45,46] In a recent prospective study of 198 patients undergoing elective major noncardiac surgery, Carliner et al[11] found that ST-T abnormalities and intraventricular conduction delay (IVCD) (QRS greater than or equal to 0.10 seconds) occurred more frequently in those with complicated versus uncomplicated courses (82 versus 59 per cent and 24 versus 7 per cent, respectively). ST-T abnormalities were sensitive (82 per cent) but not specific (41 per cent), while IVCD was specific (93 per cent) but not sensitive (24 per cent). The large number of false positives associated with ST-T abnormalities and false negatives associated with IVCD make these findings of little value in directing a more detailed preoperative work-up. Indeed, although 63 per cent of these patients had an abnormal ECG, only 3 per cent had major cardiac complications. Further prospective studies are needed to assess the impact of new ECG findings on clinical management.

Evidence of recent myocardial infarction may place the patient at increased risk for reinfarction in the postoperative period.[25,36,47] Data from the Framingham study indicate that more than 25 per cent of all infarctions are clinically silent, being detected only by routine biennial ECGs.[29] Thus, it is reasonable to screen all patients at risk (men over 40 and postmenopausal women).

Studies of vascular surgery patients suggest that an ischemic response or low exercise capacity on treadmill testing is predictive of poor outcome. Cutler et al[16] found the highest infarction and mortality rate in this group (a 27 per cent infarction rate, and a 19 per cent mortality rate), with intermediate risk in patients with an ischemic response but normal exercise capacity or in those with low exercise capacity alone. No complications occurred in patients with a normal test. Von Knorring,[55] in a prospective study of 105 patients exercised on a low-level protocol, reported a positive ischemic response in 25 per cent of patients. In this group, there was a 69 per cent perioperative cardiac complication rate, consisting primarily of transient intraoperative and postoperative ischemic ECG changes. Carliner et al[10] found *routine* exercise testing in a relatively low-risk group to be no more predictive than changes on a resting preoperative 12-lead ECG. Gerson et al[22] found the inability to exercise for more than 2 minutes to be the most sensitive predictor of outcome in elderly patients undergoing major surgery. These studies provide suggestive, but by no means conclusive, evidence that limited exercise capacity or markedly positive preoperative stress tests identify a subgroup of patients at increased risk for perioperative complications presumably due to advanced CAD or markedly impaired ventricular function.

Currently, there are few studies that have evaluated the importance of the preoperative ischemic pattern (the frequency, duration, and magnitude of ischemic episodes) detected by ambulatory ST-segment monitoring. In patients on maximal medical therapy about to undergo coronary artery bypass grafting, we have shown that 42 per cent of preoperative patients had ECG ischemic episodes, 87 per cent of which were clinically silent.[32] In this group, intraoperative ischemia was over four times more common than in those without preoperative ischemia. Assessment of a patient's ischemic pattern may have significant implications for preoperative medical therapy. As well, introduction of microprocessor driven, interactive, real-time ambulatory ST-segment monitors capable of on-line digitization and analysis of ischemic episodes with sophisticated disclosure capabilities will undoubtedly accelerate research in this area.[2]

MYOCARDIAL PERFUSION IMAGING

Intravenous injection of short-lived cationic radioisotopes, extracted from the bloodstream and transported into viable cells by the membrane sodium-potassium adenosine triphosphatase pump system, allows evaluation of cellular viability and regional blood flow.[5,52] Thallium 201, with a half-life of 72 hours, is most commonly used for imaging. Other shorter lived isotopes, such as rubidium 81, which allow more frequent repeated measurements, are available only in research settings.[50] The extraction of thallium 201 from blood is linearly related to blood flow. Thus, shortly after injection it is rapidly distributed throughout the myocardium in proportion to regional coronary blood flow. Marked reduction in regional blood flow will result in a defect on initial (early) imaging. Differences in the rate of thallium clearance between normal (rapid clearance) and underperfused (slower clearance) areas result in the phenomenon of redistribution. This is defined as a relative increase in regional thallium concentration in images obtained several hours after injection. A defect present on initial imaging that does not redistribute on delayed imaging is believed to represent an infarcted region. However, false-positive results can occur (that is, in cardiomyopathies).[52] Areas exhibiting redistribution are believed to represent ischemic or "jeopardized areas" of myocardium.

The ability of thallium imaging to distinguish between a region with a significant coronary stenosis and one without is dependent on the difference in regional flow between the two zones.[27] At rest, coronary blood flow may remain normal distal to the stenosis, even when diameter narrowing is reduced by 85 to 90 per cent. Thus, no defect will be evident on the thallium image in the distribution of the diseased vessel. However, with coronary vasodilation (exercise, ischemia, or with vasodilators such as adenosine or dipyridamole), the ability of the compromised region to increase flow (coronary vascular reserve) is severely limited and disparity in regional flow occurs. This allows differentiation between zones on imaging. In general, a 2 to 1 flow ratio between zones is required when using thallium. As little as a 15 per cent difference can be detected using more sophisticated techniques such as positron imaging. Therefore, imaging performed at rest will have very low sensitivity, while that done after exercise stress or pharmacologic vasodilation has much greater sensitivity. Guidelines for the optimal use of this technology have recently been published.[41]

DIPYRIDAMOLE THALLIUM IMAGING

Theoretical Basis

Dipyridamole is a potent coronary vasodilator when given intravenously (0.56 mg per kg over 4 minutes) or even orally in the appropriate dosage (300 mg). Coronary blood flow may increase 2.4 to 5 times from the baseline value with only a slight increase in cardiac output (1.3 times). These findings contrast with the threefold maximal increase possible with maximal exercise stress (which requires a three- to fivefold increase in cardiac output).[48] These features have made this test an attractive alternative to exercise stress testing in patients who cannot exercise due to orthopedic limitation, severe claudication, or in those with limited ability to increase cardiac output. With the use of dipyridamole, redistribution may occur with lesions as small as 40 to 60 per cent diameter narrowing.[27] A unique feature of the action of dipyridamole on the coronary circulation is the complete antagonism of its vasodilation by low doses of intravenous aminophylline (50 to 125 mg). A schematic representation of the testing protocol along with an actual scan showing redistribution is shown in Figures 1 and 2.

Clinical Studies

Medical Populations. The popularity of this test has increased dramatically since its predictive value over a number of predischarge clinical variables was demonstrated by Leppo et al in survivors of acute myocardial infarction.[33] The probability of adverse outcome was elevated fivefold in patients with redistribution. Although the test was extremely sensitive in predicting poor outcome (92 per cent), its specificity was low (44 per cent). However, of the 24 patients subsequently

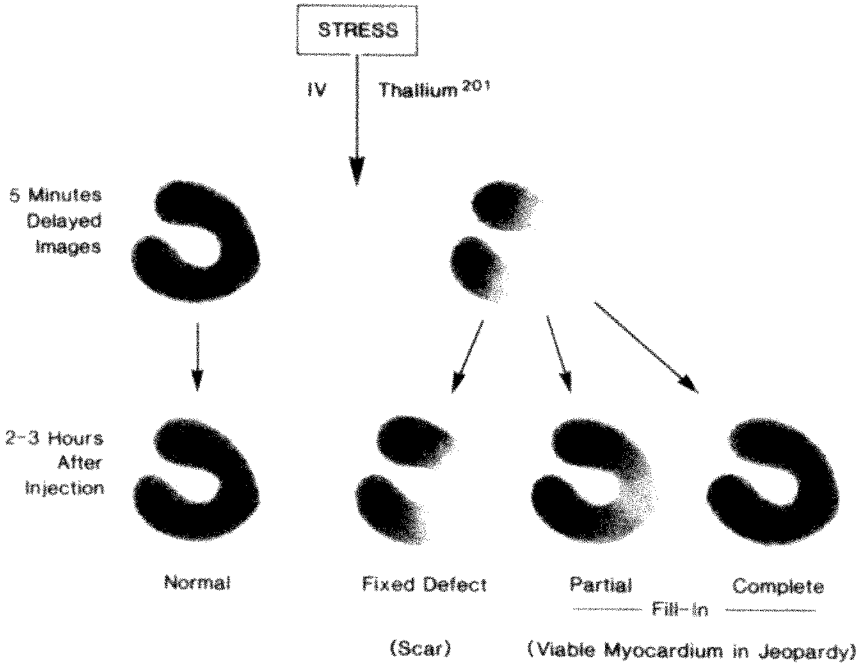


Figure 1. A representative testing protocol for dipyridamole-thallium imaging with all possible results is shown. Following administration of dipyridamole (0.56 mg per kg over 4 minutes), thallium 201 is injected (usually within 3 to 5 minutes) and imaging is begun (depicted here as 5 minutes delayed images). The patient then returns after 2 to 3 hours for the late delayed imaging by which time redistribution will have had time to occur. (*From* Brewster DC, Okada RD, Strauss HW, et al: Selection of patients for preoperative coronary angiography: Use of dipyridamole-stress-thallium myocardial imaging. J Vasc Surg 2:504–510, 1985; with permission.)

readmitted for angina, 22 exhibited redistribution on their predischarge scan.

In clinical studies, the sensitivity of the test for detecting CAD ranges from 85 to 93 per cent with a specificity from 64 to 80 per cent. Because the uptake and clearance of thallium have been found to differ from thallium kinetics during exercise stress, computerized quantitation used to enhance the sensitivity of exercise-thallium studies is not possible.[48] Thus, at the present time, interpretation is limited to a qualitative analysis.

Although the test has been found to be relatively safe, side effects, and in rare instances, major complications can occur. Thus, adherence to the same safety guidelines as exercise stress testing is recommended.[49] In the largest reported series to date (n = 239), Homma et al[28] reported chest pain in 26 per cent, ischemic ST depression in 20 per cent, and transient arrhythmias in 19 per cent. Aminophylline was required in 70 per cent of those with chest pain. Noncardiac side effects, including headache, dizziness, and nausea, were present in 4 to 11 per cent. In patients taking aminophylline, it must be held for at

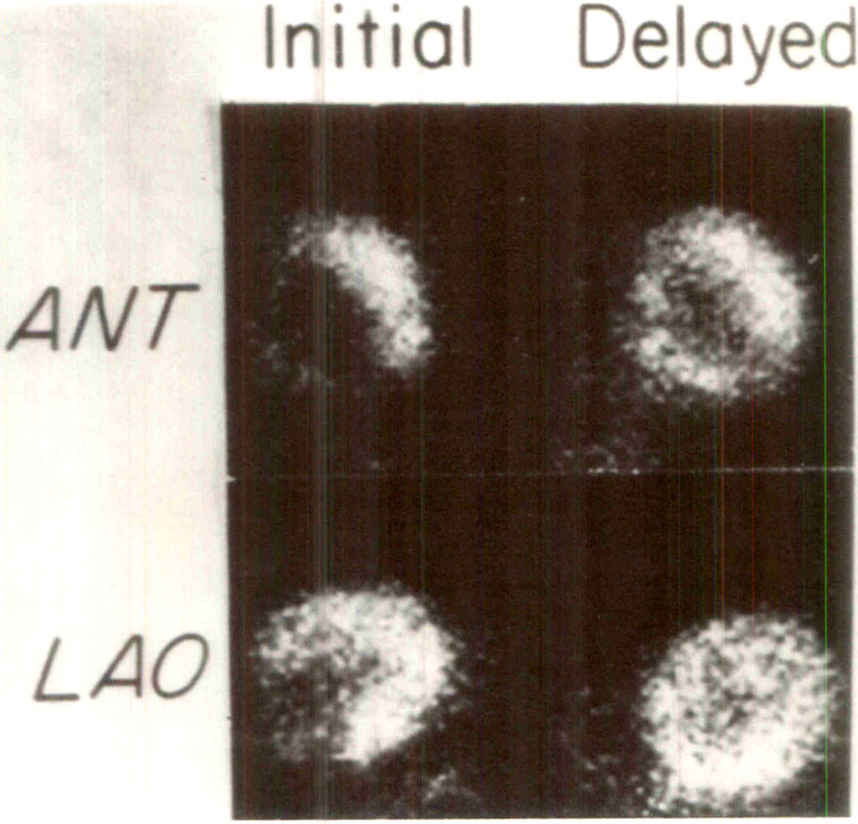


Figure 2. Actual dipyridamole-thallium scan illustrating an area of redistribution of "jeopardized myocardium" (inferoapical region). ANT = anterior view, LAO = left anterior oblique view. (*From* Brewster DC, Okada RD, Strauss HW, et al: Selection of patients for preoperative coronary angiography: Use of dipyridamole-stress-thallium myocardial imaging. J Vasc Surg 2:504–510, 1985; with permission.)

least 24 hours before the test, and pulmonary function may worsen. In this series one patient developed severe bronchospasm, although there were no deaths or myocardial infarctions. This group now routinely administers aminophylline (50 mg) 20 minutes into the study (after peak vasodilation) in all patients. Ventricular fibrillation in one patient, and severe myocardial ischemia requiring emergency coronary angioplasty in another, have also been reported anecdotally.[4,35]

Hemodynamic effects of dipyridamole include a mild decrease in systolic blood pressure (mean 12 mm Hg) and increase in heart rate (mean 9 bpm) occurring 6 minutes after injection.[28] In an elderly population (54 patients over age 65), attenuation of the heart rate response as well as a delayed decrease in systolic pressure has been noted. Suprisingly, the incidence of side effects was similar to that of a group of younger patients.[23]

Surgical Populations. The value of this test in vascular surgery patients who are at increased risk for perioperative cardiac complications has been assessed at several centers. The results of four clinical series are summarized in Table 1. Although all are prospective, none were blinded or randomized, which complicates their interpretation.

Boucher et al[8] studied patients with stable CAD undergoing elective vascular surgery. Those with recent myocardial infarction, unstable angina, congestive heart failure, or severe systemic illness were excluded. Six patients underwent preoperative coronary angiography based on the abnormal scan results. Of the remaining 48, 16 had thallium redistribution and 12 had persistent defects. All eight cardiac events (myocardial infarction or unstable angina) occurred in those with redistribution. No events occurred in patients with normal scans or persistent defects. Thus, while the test was very sensitive (100 per cent) and specific (80 per cent), its positive predictive value was low (50 per cent). However, exclusion of the six patients before surgery, all of whom had multivessel disease, may have been responsible in part for the low predictive value (that is, these patients might have had complications).

Cutler and Leppo[17] found that all postoperative events (nine myocardial infarctions with no deaths) were predicted when the scan demonstrated two or more ischemic segments. Patients with one ischemic segment, partial redistribution, or persistent defects were not at increased risk. No events occurred in the 62 patients with normal scans. Based on clinical and scan results, 20 patients underwent preoperative angiography. Of these, the six with the greatest number of ischemic segments underwent coronary artery bypass grafting, with one death after coronary artery bypass grafting, while one died from a ruptured aneurysm before coronary artery bypass grafting, and nine had no operation. Surprisingly, the infarction rate for patients undergoing aortic vascular surgery in this series (26 per cent) was very high.

Leppo et al[34] compared the utility of this test with exercise treadmill testing as well as other clinical variables. Fourteen of the 15 myocardial infarctions occurred in patients with redistribution, three of whom had positive treadmill tests. Of the 89 patients who underwent surgery, thallium redistribution was the most significant predictor of risk, although ST depression during dipyridamole infusion and a history of diabetes were weaker yet independent predictors. All three factors increased the relative risk 30-fold. Thallium redistribution was found to be more sensitive than abnormal results on exercise testing. Surprisingly, none of the clinical variables correlated with the presence of thallium redistribution.

Eagle et al[20] tested its role as a routine screening test in patients undergoing vascular surgery. They concluded that it is best reserved for patients with one or more clinical risk factors (angina, history of infarction, congestive heart failure, diabetes, or Q wave on ECG). In a validation set of 50 patients, there were no postoperative ischemic events in 6 of the 23 low-risk patients with redistribution. In the 27

Table 1. *Perioperative Studies Using Dipyridamole-Thallium Imaging*

				CARDIAC COMPLICATIONS (%): INCIDENCE AND PREDICTION					
AUTHOR	STUDY PERIOD	INCLUSION CRITERIA	N	UA	MI	DEATH	SENS	SPEC	PPV
Boucher, 1985	1982–84	Stable CAD, elective vascular, no recent MI	54 studied 48 operated 6 to CABG	10.4	6.3	2.1	100	80	50
Cutler, 1987	NS	Elective vascular, no recent MI	116 studied 106 operated 6 to CABG	0	8.5	0	100	61	17
Leppo, 1987	1984–85	Elective vascular, no recent MI	100 studied 89 operated 6 to CABG	0	17	1	93	53	33
Eagle, 1987	1985	Elective vascular, no recent MI	111 studied 111 operated 0 to CABG	10	5.4	4.5	89	72	38

Predictive indices calculated from clinical data using standard formulas.

Sensitivity (positivity in disease), true positive/(true positive + false negative). Specificity (negativity in health), true negative/(true negative + false positive). Positive predictive value, true positive/(true positive + false positive).

NS = not specified, UA = unstable angina, MI = myocardial infarction, Sens = sensitivity, spec = specificity, PPV = positive predictive value, CABG = coronary artery bypass graft.

with clinical risk factors, 8 of 18 with redistribution had adverse outcomes. In contrast to the findings of Cutler et al, analysis of the pattern or degree of redistribution added little to prediction.[17]

These studies suggest that redistribution on dipyridamole thallium imaging is a sensitive predictor of adverse outcome. However, its ultimate value will be dependent on the complication rates present at a given institution. In settings with low complication rates (lower than those in Table 1), it is less likely to be of value. The low specificity (high false-positive rate) suggests that other key factors in addition to ischemia, as yet undetermined, are important. Indeed, none of these studies has assessed the importance of the intraoperative and early postoperative period. Our preliminary studies in high-risk patients primarily undergoing vascular surgery suggest that either fixed or redistributed segments are sensitive indicators for the development of intraoperative ischemia, detected by continuous 12-lead electrocardiography or two-dimensional transesophageal echocardiography.[38]

ASSESSING LEFT VENTRICULAR EJECTION FRACTION

Theoretical Basis

Although left ventricular function can be assessed by physical examination, chest roentgenogram, or precordial echocardiography, radionuclide methods are the most accurate and are easily performed. The most commonly used technique, equilibrium gated blood pool radionuclide angiography, uses the multigated acquisition approach (MUGA) to provide composite images over a 2- to 10-minute period by gating to the QRS complex.[41] It allows determination of right and left ventricular volume, ejection fraction, regional wall motion, and pulmonary blood volume. The use of technetium-labeled red blood cells allows imaging over several hours. Less commonly used is "first pass" radionuclide angiography, which uses rapidly acquired image frames to trace a bolus of technium 99 as it passes through the right and left heart. Due to the rapid disappearance of the technetium 99, this method allows repeated injections over short time periods. Thus, the effects of acute maneuvers may be better observed. Since gated blood pool imaging provides higher resolution images, it is more widely used.

Clinical Studies

There is abundant evidence demonstrating that impairment of left ventricular function following acute myocardial infarction is associated with poor long-term survival. The Multicenter Postinfarction Research Group followed 866 patients from 1 to 3 years postinfarction.[39,53] Four independent predictors of mortality were identified, three of which are measures of ventricular function: advanced New York Heart Association Classification prior to infarction, rales in upper lung fields while in the Critical Care Unit, and radionuclide ejection fraction less than 0.40 prior to discharge. The fourth, ventricular ectopy of 10 or more per hour, although statistically independent, imparts lower risk. Patients with the two strongest risk factors, rales and ejection fraction less than 0.40, had an eightfold mortality risk and those with four factors, a 2-year mortality of 60 per cent (Fig. 3). Even in patients with resting ejection fraction greater than 0.40, the inability to maintain or to increase ejection fraction by at least 0.05 predicts the presence of multivessel CAD.

In surgical patients, indirect measurements of ventricular function such as physical signs of congestive heart failure are significant predictors. Goldman found an S_3 gallop or the presence of jugular venous distention to be the most important of the multivariate predictors.[25] Curiously, other signs and symptoms consistent with congestive heart failure, most notably cardiomegaly, were insignificant. In this series, postoperative pulmonary edema in elderly pa-

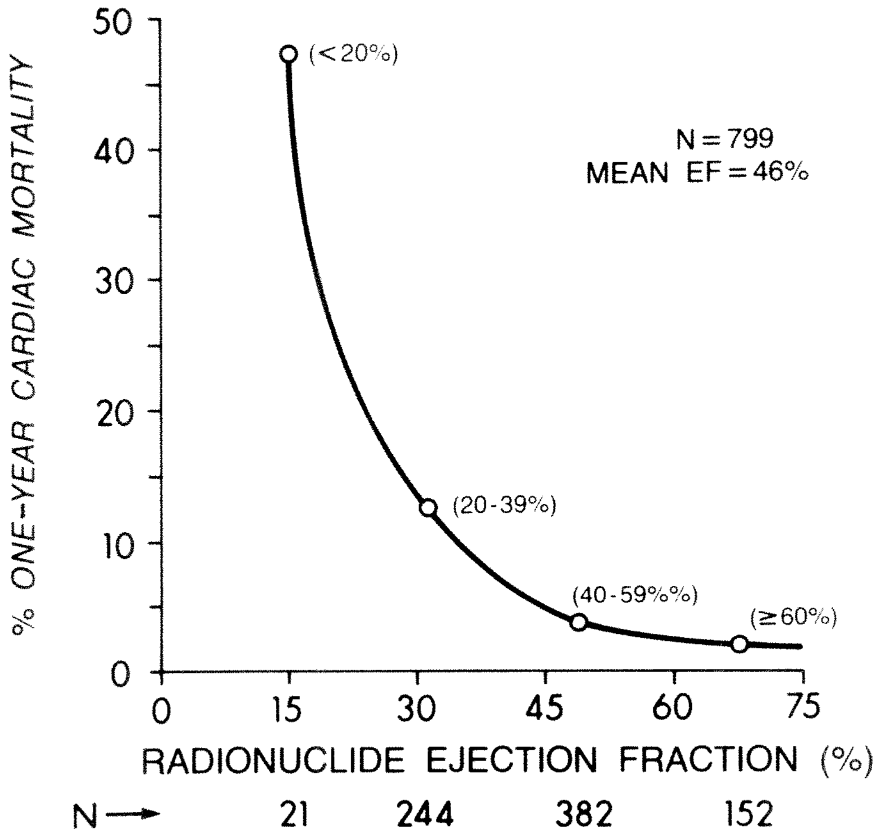


Figure 3. The importance of ventricular function, determined prior to hospital discharge, in determinig long-term survival in a large series of medical patients following acute myocardial infarction is illustrated. (*From* The Multicenter Postinfarction Research Group: Risk stratification and survival after myocardial infarction. N Engl J Med 309:331–336, 1983; with permission.)

tients undergoing aortic vascular or abdominal surgery was associated with a 40 per cent cardiac mortality. Patients with prior infarction, congestive heart failure, and concurrent angina have been shown to be at substantially increased risk for recurrent postoperative infarction.[47]

Several recent studies have documented the importance of left ventricular ejection fraction in predicting outcome. In two series, Pasternack and coworkers reported on a total of 150 patients undergoing either abdominal aortic aneurysm resection (n = 50) or lower extremity revascularization (n = 100) who had preoperative determination of ejection fraction.[42,43] Ejection fraction was found to be a sensitive predictor of outcome (Fig. 4). There were no postoperative infarctions in patients with ejection fraction greater than 55 per cent. In those with ejection fraction from 55 to 35 per cent, 19 per cent had myocardial infarction (one death) and in those with ejection fraction from 35 to 25 per cent, 77 per cent had myocardial infarction (two deaths). However, it is interesting that all but one of the myocardial infarctions were nontransmural and the mortality rate (3/22 = 14 per cent) was very low for this setting. Gerson et al[22] prospectively studied 155 asymptomatic patients over the age of 65 undergoing elective abdominal or thoracic surgery. On univariate analysis resting ejection fraction less than 35 per cent was a significant risk factor, while multivariate analysis confirmed only the inability to exercise for 2 minutes to raise the heart rate above 99 bpm as significant. Although the median ejection fraction in patients with cardiac complications was lower (42 per cent) than in those without (63 per cent), there was substantial overlap. Thus, ejection fraction may be a more sensitive predictor in vascular surgery patients than in general surgery patients.

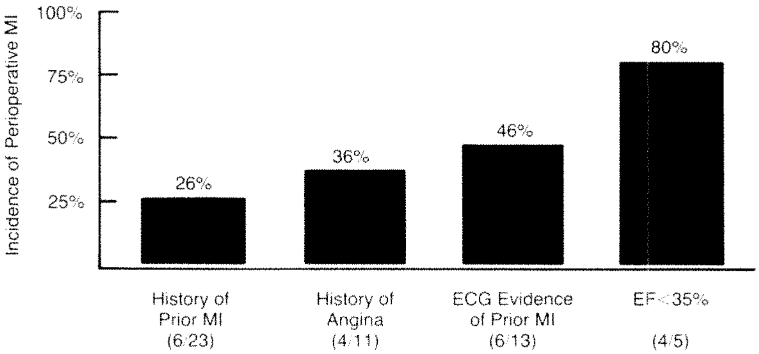


Figure 4. The incidence of clinical risk factors and ejection fraction determined by radionuclide angiography (MUGA) among the eight patients who developed postoperative myocardial infarction following abdominal aortic aneurysm (total n = 50) is shown. The fractions represent the number of patients with MI divided by the total number of patients in the series with that risk factor. (*From* Pasternack PF, Imparato AM, Bear G, et al: The value of radionuclide angiography as a predictor of perioperative myocardial infarction in patients undergoing abdominal aortic aneurysm resection. J Vasc Surg 1:320–325, 1984; with permission.)

Once reduced ejection fraction is detected, attempts should be made to optimize ventricular function using standard medical therapy (digoxin, diuretics, vasodilators). In patients with associated three vessel CAD, in whom chronic ischemia may cause chronic ventricular dysfunction, myocardial revascularization has been shown to enhance survival and should be considered preoperatively. Patients undergoing major procedures (intra-abdominal, aortic vascular, or intrathoracic) should be monitored closely with intra-arterial and pulmonary artery catheters intraoperatively and postoperatively. Acute rise in pulmonary artery wedge pressure, which may reduce coronary perfusion pressure and cause subendocardial ischemia, should be avoided and if it occurs, aggressively treated. The selective use of vasodilators such as nitroglycerin, alone or in combination with inotropes, may be indicated.

Several studies suggest that aggressive preoperative monitoring protocols including pulmonary artery catheterization and cautious volume loading, may enhance preoperative ventricular function and decrease postoperative morbidity in high-risk patients (vascular surgery or elderly patients). However, the uncontrolled, nonrandomized design of these studies greatly limits their interpretation.[1,19,51] The added cost of additional intensive care utilization as well as the hemodynamic and psychological stimulation associated with catheterization and intensive care stay have not been adequately evaluated. In general, we limit this type of intervention to patients with poorly controlled congestive heart failure requiring urgent or semiurgent aortic or lower extremity revascularization. Further prospective, randomized studies are needed to resolve this issue.

SUMMARY

Clinicians have available to them a variety of preoperative screening and monitoring techniques allowing detection of CAD, infarction, and evaluation of ventricular function, factors that have been shown to correlate with postoperative cardiac morbidity. Electrocardiography has been the traditional mainstay for detecting CAD. The increasing use of ambulatory ST-segment monitoring should ensure its importance for the foreseeable future. The use of techniques that unmask CAD by increasing myocardial oxygen demand, or by use of pharmacologic vasodilation to induce regional differences in coronary blood flow, have greater sensitivity than tests performed in the resting state. Dipyridamole-thallium imaging, attractive due to its application to patients unable to exercise, has grown in popularity. Although it may be a sensitive predictor of adverse outcome or intraoperative ischemia, evidence suggests that it has little value as a routine screening tool. Evaluation of left ventricular function is possible using many different techniques, although radionuclide angiography is the most sensitive. Low ejection fraction, especially below 0.40, identifies a subgroup of patients at high risk. Aggressive therapy of myocardial ischemia or congestive heart failure, identified by these techniques, may enhance perioperative survival in these patients. Preoperative assessment remains the cornerstone of perioperative care.

REFERENCES

1. Babu SC, Sharma P, Raciti A, et al: Monitor-guided responses. Operability with safety is increased in patients with peripheral vascular diseases. Arch Surg 115:1384–1386, 1980
2. Barry J, Campbell S, Nabel EG, et al: Ambulatory monitoring of the digitized electrocardiogram for detection and early warning of transient myocardial ischemia in angina pectoris. Am J Cardiol 60:483, 1987
3. Bär FW, Brugada P, Dassen WR, et al: Prognostic value of Q waves, R/S ratio, loss of R wave voltage, ST-T segment abnormalities, electrical axis, low voltage and notching: Correlation of electrocardiogram and left ventriculogram. J Am Coll Cardiol 4:17–27, 1984
4. Bayliss J, Pearson M, Sutton GC: Ventricular dysrhythmias following intravenous dipyridamole during "stress" myocardial imaging. Br J Radiol 56:686, 1983
5. Berger HJ, Zaret BL: Nuclear Cardiology (medical progress). N Engl J Med 305:799–807, 1981
6. Berman DS, Rozanski A, Knoebel SB: The detection of silent ischemia: Cautions and precautions. Circulation 75:101–105, 1987
7. Biagini A, Mazzei MG, Carpeggiani C, et al: Vasospastic ischemic mechanism of frequent asymptomatic transient ST-T changes during continuous electrocardiographic monitoring in selected unstable angina patients. Am Heart J 103:13–20, 1982
8. Boucher CA, Brewster DC, Darling RC, et al: Determination of cardiac risk by dipyridamole-thallium imaging before peripheral vascular surgery. N Engl J Med 312:389–394, 1985
9. Brewster DC, Okada RD, Strauss HW, et al: Selection of patients for preoperative coronary angiography: Use of dipyridamole-stress-thallium myocardial imaging. J Vasc Surg 2:504–510, 1985
10. Carliner NH, Fisher ML, Plotnick GD, et al: Routine preoperative exercise testing in patients undergoing major noncardiac surgery. Am J Cardiol 56:51–57, 1985
11. Carliner NH, Fisher ML, Plotnick GD, et al: The preoperative electrocardiogram as an indicator of risk in major noncardiac surgery. Can J Cardiol 2:134–137, 1986
12. Chaitman BR, Hanson JS: Comparative sensitivity and specificity of exercise electrocardiographic lead systems. Am J Cardiol 47:1335–1349, 1981
13. Chaitman BR, Waters DD, Theroux P, et al: S-T segment elevation and coronary spasm in response to exercise. Am J Cardiol 47:1350–1358, 1981
14. Chaitman BR: The changing role of the exercise electrocardiogram as a diagnostic and prognostic test for chronic ischemic heart disease. J Am Coll Cardiol 8:1195–1210, 1986
15. Chierchia S, Lazzari M, Freedman B, et al: Impairment of myocardial perfusion and function during painless myocardial ischemia. J Am Coll Cardiol 1:924–930, 1983
16. Cutler BS, Wheeler HB, Paraskos JA, et al: Applicability and interpretation of electrocardiographic stress testing in patients with peripheral vascular disease. Am J Surg 141:501–505, 1981
17. Cutler BS, Leppo JA: Dipyridamole thallium 201 scintigraphy to detect coronary artery disease before abdominal aortic surgery. J Vasc Surg 5:91–100, 1987
18. Deanfield JE, Selwyn AP, Chierchia S, et al: Myocardial ischaemia during daily life in patients with stable angina: Its relation to symptoms and heart rate changes. Lancet 1:753–758, 1983
19. Del Guercio LRM, Cohn JD: Monitoring operative risk in the elderly. JAMA 243:1350–1355, 1980

20. Eagle KA, Singer DE, Brewster DC, et al: Dipyridamole-thallium scanning in patients undergoing vascular surgery. Optimizing preoperative evaluation of cardiac risk. JAMA 257:2185–2189, 1987
21. Fuchs RM, Achuff SC, Grunwald J, et al: Electrocardiographic localization of coronary artery narrowings: Studies during myocardial ischemia and infarction in patients with one-vessel disease. Circulation 66:1168–1176, 1982
22. Gerson MC, Hurst JM, Hertzberg VS, et al: Cardiac prognosis in noncardiac geriatric surgery. Ann Intern Med 103:832–837, 1985
23. Gerson MC, Moore EN, Ellis K: Systemic effects and safety of intravenous dipyridamole in elderly patients with suspected coronary artery disease. Am J Cardiol 60:1399–1401, 1987
24. Goldberger AL: Electrocardiogram in coronary artery disease: Limitations in sensitivity. *In* Myocardial Infarction: Electrocardiographic Differential Diagnosis. St. Louis, C.V. Mosby, 1984, pp 303–308
25. Goldman L, Caldera DL, Southwick FS, et al: Cardiac risk factors and complications in non-cardiac surgery. Medicine 57:357–370, 1978
26. Gottlieb SO, Weisfeldt ML, Ouyang P, et al: Silent ischemia as a marker for early unfavorable outcomes in patients with unstable angina. N Engl J Med 314:1214–1219, 1986
27. Gould LK: Pharmacologic intervention as an alternative to exercise stress. Sem Nucl Med 17:121–130, 1987
28. Homma S, Gilliland Y, Guiney TE, et al: Safety of intravenous dipyridamole for stress testing with thallium imaging. Am J Cardiol 59:152–154, 1987
29. Kannel WB, Abbott RD: Incidence and prognosis of unrecognized myocardial infarction: An update on the Framingham Study. N Engl J Med 311:1144–1147, 1984
30. Karnegis JN, Matts J, Tuna N, et al: Relation between Q-QS changes on the rest electrocardiogram and left ventricular function with healed myocardial infarction. Am J Cardiol 58:399–405, 1986
31. Killip T, Ryan TJ: Randomized trials in coronary bypass surgery. Circulation 71:418–421, 1985
32. Knight A, Hollenberg M, London MJ, et al: Perioperative myocardial ischemia: Importance of the preoperative ischemic pattern. Anesthesiology 68:681–688, 1988
33. Leppo JA, O'Brien J, Rothendler JA, et al: Dipyridamole-thallium-201 scintigraphy in the prediction of future cardiac events after acute myocardial infarction. N Engl J Med 310:1014–1018, 1984
34. Leppo J, Plaja J, Gionet M, et al: Noninvasive evaluation of cardiac risk before elective vascular surgery. J Am Coll Cardiol 9:269–276, 1987
35. Lewen MK, Labovitz AJ, Kern MJ, et al: Prolonged myocardial ischemia after intravenous dipyridamole thallium imaging. Chest 92:1102–1104, 1987
36. London MJ, Mangano DT: Assessment of perioperative risk. *In* Stoelting RK, Barash PG, Gallagher TJ (eds): Advances in Anesthesia, vol 5. Chicago, Year Book Medical, 1988, p 53
37. London MJ, Hollenberg M, Wong MG, et al: Intraoperative myocardial ischemia: Localization by continuous 12-lead electrocardiography. Anesthesiology 69:232–241, 1988
38. London MJ, Tubau JF, Harris D, et al: Dipyridamole thallium imaging predicts intraoperative ischemia in patients undergoing major vascular surgery [abstract]. J Am Coll Cardiol 11:162A, 1988
39. Moss AJ, Bigger JT, Odoroff CL: Postinfarct risk stratification. Prog Cardiovasc Dis 24:389–412, 1987
40. Nabel EG, Rocco MB, Selwyn AP: Characteristics of ischemia detected by ambulatory electrocardiographic monitoring. Circulation 75(suppl V):74, 1987
41. O'Rourke RA, Chatterjee K, Dodge HT, et al: Guidelines for clinical use of cardiac radionuclide imaging December 1986: A report of the American College of Cardiology/American Heart Association Task Force on Assessment of Cardiovascular Procedures (Subcommittee on Nuclear Imaging). Circulation 74:1469A–1482A, 1986
42. Pasternack PF, Imparato AM, Bear G, et al: The value of radionuclide angiography

as a predictor of perioperative myocardial infarction in patients undergoing abdominal aortic aneurysm resection. J Vasc Surg 1:320–325, 1984

43. Pasternack PF, Imparato AM, Riles TS, et al: The value of the radionuclide angiogram in the prediction of perioperative myocardial infarction in patients undergoing lower extremity revascularization procedures. Circulation 72:II13–17, 1985
44. Quyyumi AA, Mockus L, Wright C, et al: Morphology of ambulatory ST segment changes in patients with varying severity of coronary artery disease. Investigation of the frequency of nocturnal ischaemia and coronary spasm. Br Heart J 53:186–193, 1985
45. Rabkin SW, Horne JM: Preoperative electrocardiography: Its cost-effectiveness in detecting abnormalities when a previous tracing exists. Can Med Assoc J 121:301–306, 1979
46. Rabkin SW, Horne JM: Preoperative electrocardiography: Effect of new abnormalities on clinical decisions. Can Med Assoc J 128:146–147, 1983
47. Rao TK, Jacobs KH, El-Etr AA: Reinfarction following anesthesia in patients with myocardial infarction. Anesthesiology 59:499–505
48. Ruddy TD, Gill JB, Finkelstein DM, et al: Myocardial uptake and clearance of thallium-201 in normal subjects: Comparison of dipyridamole-induced hyperemia with exercise stress. J Am Coll Cardiol 10:547–556, 1987
49. Schlant RC, Blomqvist CG, Brandenburg RO, et al: Guidelines for exercise testing: A report of the Joint American College of Cardiology/American Heart Association Task Force on Assessment of Cardiovascular Procedures (Subcommittee on Exercise Testing). Circulation 74:653A–67A, 1986
50. Shea MJ, Wilson RA, deLandsheere K, et al: Use of short- and long-lived rubidium tracers for the study of transient ischemia. J Nucl Med 28:989–997, 1987
51. Skillman JJ, Patel RC, Klick JM: Cardiac performance testing by volume loading and lower-extremity compression. Arch Surg 117:1009–1011, 1982
52. Strauss HW, Boucher CA: Myocardial perfusion studies: Lessons from a decade of clinical use. Radiology 160:577–584, 1986
53. The Multicenter Postinfarction Research Group: Risk stratification and survival after myocardial infarction. N Engl J Med 309:331–336, 1983
54. Uusitupa M, Pyorala K, Raunio H, et al: Sensitivity and specificity of Minnesota Code Q-QS abnormalities in the diagnosis of myocardial infarction verified at autopsy. Am Heart J 106:753–757, 1983
55. von Knorring J, Lepantalo M: Prediction of perioperative cardiac complications by electrocardiographic monitoring during treadmill exercise testing before peripheral vascular surgery. Surgery 99:610–613, 1986

Anesthesia (129)
San Francisco Veterans Administration Medical Center
4150 Clement Street
San Francisco, CA 94121

Electrical Safety and Device Calibration

J. C. Horrow, MD, and David T. Seitman, MD†*

The safety of electrical energy is taken for granted. This lax attitude has been made possible by the efforts of many safety and regulatory agencies that oversee the aspects of electrical power supply, wiring, and device construction. Based on the safety of household electricity, one can understand the confidence with which physicians have embraced use of electrically powered devices in the operating room environment in the last 15 years. But the hazard of electric shock to patients and to operating room personnel is not insignificant. Therefore, additional measures have been undertaken to increase safety in the operating room. To understand the nature of and rationale for the special electrical construction in the operating room, we must first review the scientific basis of electric power, the pathophysiology of electrocution, and how electricity is supplied to households and hospitals.

THE BASIS OF ELECTRICITY

Current flows only when a circuit is closed. A closed circuit provides an unbroken loop-like path for electrons to travel from their source and back to it. The magnitude of current, measured in coulombs per second, or Amperes, depends on the driving "force" for electrons (the voltage) and the resistance to current flow, measured in ohms. This is analogous to the well-known simplified expression for the flow of blood in the body: cardiac output in liters per minute equals the net driving pressure (mean arterial pressure less central venous pressure) divided by the resistance to flow (systemic vascular resistance) (Fig. 1).

One can touch a source of high potential with impunity as long as *no* path exists for current to return to its source. It is easy to under-

---

Hahnemann University, Philadelphia, Pennsylvania

*Associate Professor of Anesthesiology
†Senior Instructor of Anesthesiology

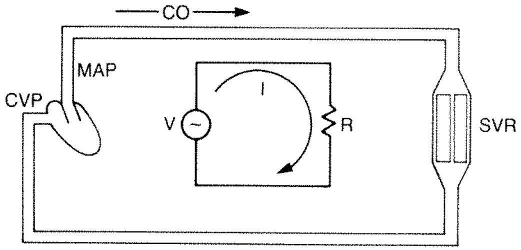


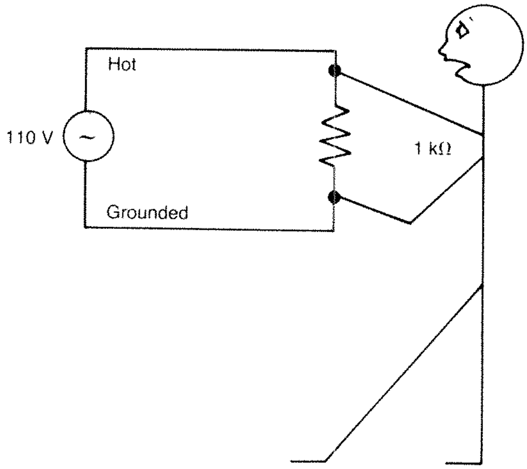
Figure 1. The cardiovascular analogy of Ohm's law. The potential difference across a voltage source, designated here as V volts, is analogous to the pressure differential (MAP-CVP) driving blood through the body. The device load (R) measured in ohms, is analogous to the resistance to flow provided by the vasculature, the systemic vascular resistance (SVR). Electrical charge (measured in coulombs) and liters of blood are analogues. Liters of blood flow per minute, the cardiac output (CO), corresponds to the flow of charge (I) measured in coulombs per second, or amperes. Just as CO = (MAP-CVP)/SVR, in the electrical circuit I = V/R.

stand the path current takes when one grips the "hot" power wire in one hand and the grounded one in the other (Fig. 2). Since our devices are powered by alternating current (AC), there are many instances when one would presuppose safety when in fact a hazard exists. When AC passes near electrical conductors, *capacitive coupling* occurs, creating pathways for current where none is presumed to exist (Fig. 3). All devices have a "leakage" current associated with them due to capacitive coupling. It is particularly important for a device chassis (its housing) to be electrically neutral (out of the circuit), since people touch it.

PATHOPHYSIOLOGY OF ELECTROCUTION

Electrical energy can be harmful by causing skin burns or by fibrillating the heart. The former topic will be discussed in the section

Figure 2. A complete circuit exists for current flow. Beginning at the source of power, current flows via the hot conductor wire into the victim's right hand, up the arm, across the chest, down the left arm, then via the grounded conductor wire, back to the source. The magnitude of current flow depends on the resistance provided by the victim. A transthoracic resistance of 1000 ohms is commonly obtained with wet hands. Ohm's law states that the resulting current will be 110 V/1000 ohms = 110 mA, enough potentially to cause fibrillation.



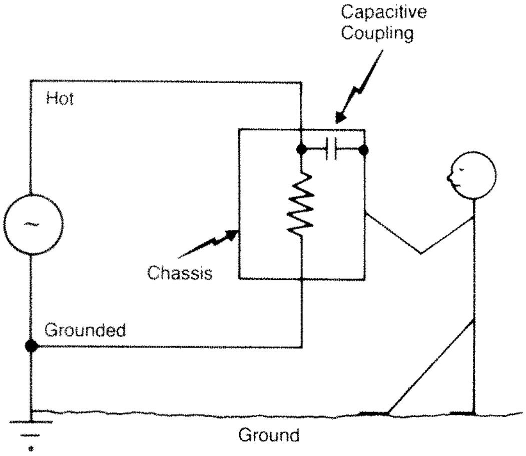


Figure 3. Two conductors in proximity form a capacitor. Although charge itself does not pass across a capacitor (unless the capacitor is damaged), alternating current flows back and forth around it. A capacitor creates a formidable barrier to flow of very low-frequency current; direct current is totally blocked. High-frequency current passes easily in circuits with capacitors. Circuit elements in devices in proximity will necessarily have capacitive coupling. Because the effective capacitance is small and the frequency relatively low (60 Hz), tiny currents are generated. They are usually of little concern.

on electrocautery. Direct current is used to defibrillate the heart. It works by the simultaneous depolarization of all myocardial tissue. Alternating current, however, can induce fibrillation.[1,8,17–21] When sufficient current of a given frequency traverses the myocardium, the orderly sequence of depolarization is disturbed, with fibrillation resulting. What constitutes a sufficient current? That depends on the entry point: for a small current applied via a fluid-filled catheter touching the myocardium, 50 μA may suffice. For currents passing through the trunk from the body surface, 100 to 2500 mA is required.[8] The threshold value of fibrillating current is also frequency dependent.[17] The heart is *most* sensitive to current at 60 Hz (Fig. 4), which is the frequency of household current. Currents smaller in magnitude than the fibrillation threshold cause other effects. For example, muscular stimulation occurs when 16 mA is applied across the trunk. Above this current level, contraction of flexors in the hands prevents an electrocution victim from releasing a gripped conductor, a vexing problem indeed!

HOUSEHOLD ELECTRICAL CONVENTIONS

Electrical power is supplied to homes, hospitals, and industry as alternating current because the loss of power over transmission lines with AC is much less than it is with direct current. Of the two power lines at the building's service entrance, one is securely attached to the ground via a water pipe or a driven conducting rod. That line is termed the "ground*ed*" line.[26] Unfortunately, this practice permits a person to form part of a circuit by touching the ungrounded line (the "hot" line) and then contacting the ground by standing in a puddle of water near a drain (Fig. 5).

What kind of safety is provided to prevent shock in households?

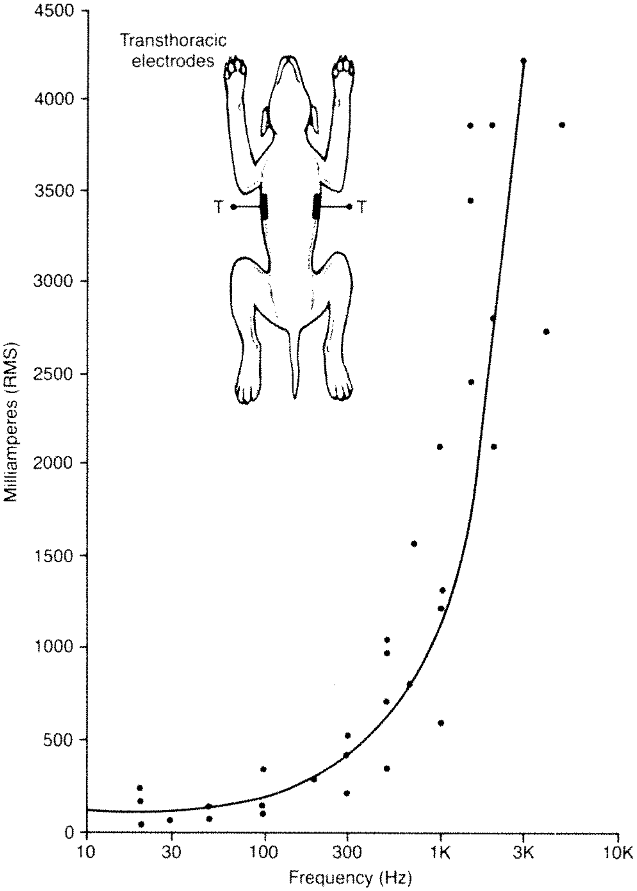


Figure 4. The threshold alternating current for fibrillation applied across transthoracic leads in a dog is plotted against the frequency of the AC applied. (*From* Geddes LA, Baker LE: Response to passage of electric current through the body. J Assoc Advance Med Instrum 5:13–18, 1971; with permission of the author and publisher.)

Fuses and circuit breakers provide protection against *fires*, not electrocution. These devices force open circuits at 15 or 20 A, whereas fibrillation occurs at 100 mA and electric shock at smaller currents. Modern wiring does require, however, a special device called a ground-fault circuit interrupter (GFCI) in high-risk locations. The GFCI measures the difference in current between the hot and the ground*ed* wires. When the difference exceeds 4 to 6 mA for more than 25 ms, the GFCI opens the circuit.[26] While shock (sensation) is not prevented, the current level is limited enough to prevent electrocution (fibrillation). Note also that 6 mA is below the "let-go" current of 16 mA. GFCIs are required by the latest electrical code in bathrooms, outdoors, and for outlets over counters that are within 6 ft of a kitchen sink. Compliance with the national code varies with location.

The code also requires that all newly installed receptacles be able

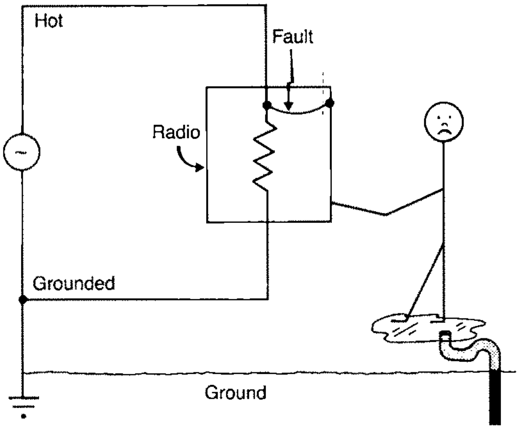


Figure 5. Current has two paths to follow in this model of electrocution. One path is through the radio. The other path is via the hot wire to the radio chassis owing to a fault in the wire, such as broken wire insulation. When the victim touches the chassis and stands in a puddle of fluid, current can continue from chassis through the trunk, via the puddle and drain, to ground. Since the grounded conductor is connected physically to ground at the service entrance, the circuit is completed via the grounded conductor back to the source of power.

to receive a third wire, called the "ground*ing*" wire. This is different from the ground*ed* wire. The ground*ing* wire provides a path for stray currents, also called leakage currents, back to the service entrance. When a ground*ing* wire is supplied in a device's power cord, the housing of that device (chassis) is connected to the ground*ing* wire to decrease the possibility of stray currents returning to the service entrance via people who touch the enclosure. The now familiar ground*ing* prong is longer than the other prongs and is somewhat rounded. At the service entrance, the ground*ing* wires are attached to the ground*ed* wires. This connection provides the complete circuit needed for stray currents to return to the source of power and trip a circuit breaker before a person can interpose himself in a hot-to-ground circuit loop and thus receive a shock.

THE HOSPITAL ELECTRICAL ENVIRONMENT

Receptacles in hospitals are similar to those in households. Certain areas however, have isolated power supplies.[8,20,24] In these areas, the connection between the ground*ed* and the ground*ing* wires is effectively removed by the use of an isolation transformer (Fig. 6). Energy is transferred through the transformer by its conversion from electrical to magnetic energy and back again. Electrical energy passes through the transformer only if a complete circuit exists from one side of the secondary winding of the transformer to the other side of the secondary winding. The advantage of this arrangement is that a fault (unwanted connection) to the chassis from either line does not result in a completed circuit. Thus, it cannot result in a large current, blown fuse, or electric shock. The circuit is incomplete because there is no electrical path through the transformer.

The isolation transformer creates an ungrounded electrical system. In the ungrounded system (Fig. 6*B*), a fault from the hot wire to

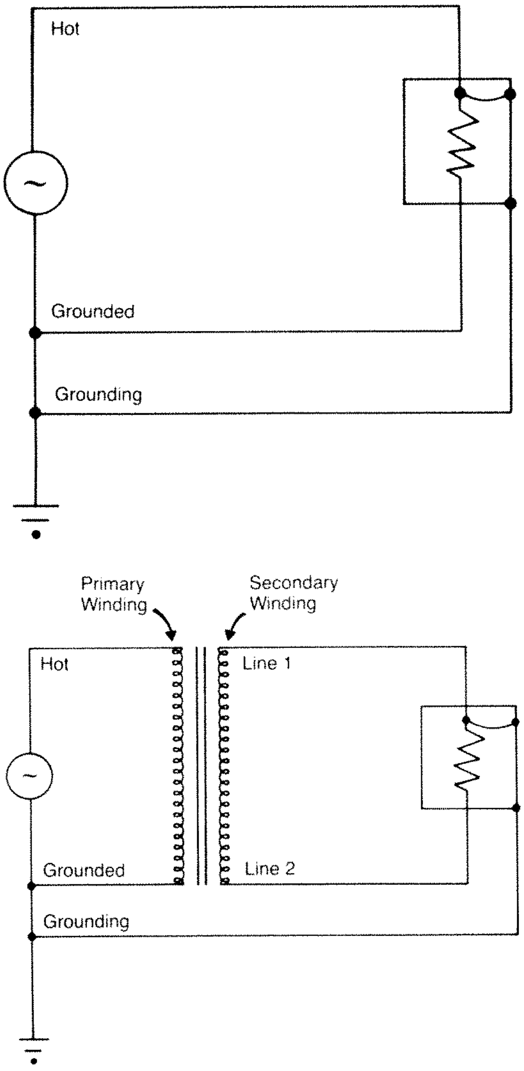


Figure 6. *A*, the grounded electrical system with ground*ing* conductor added. Note that a fault to the chassis from the hot wire results in a complete circuit, which will trip a circuit breaker, thus disabling power to all devices supplied by that breaker. The ground*ing* conductor provides a small measure of additional safety by enabling detection of the fault. However, it does so by disabling power. *B*, the isolated power supply. The isolation transformer turns the grounded system into an ungrounded system. There is now no complete path for current to follow from the secondary winding of the transformer via ground or the ground*ing* conductor back to the secondary winding. Note that, in comparison with Figure 5, a victim electrically connected to ground would not experience shock with the ungrounded system.

the chassis does not create a potential shock hazard. When a potential victim touches the chassis and stands in a pool of fluid there is no complete circuit since the ground*ing* pathway is no longer directly connected to the ground*ed* side of the circuit. In fact the distinction between hot and ground*ed* is lost, and the conductors supplied by the isolation transformer are termed "line 1" and "line 2."

However, this system is far from foolproof. The fault from line 1 to chassis referred to previously will go undetected in an ungrounded system. The device still works and no one receives a shock. But when a second fault in that device occurs, a large current can flow, causing a circuit breaker to trip and power to fail to all devices being serviced through that circuit. The isolation transformer has allowed for a single fault to occur without interrupting power or creating the potential for shock.

We somehow need to know about the first fault to ground when it occurs to prevent a later unwanted power interruption. The line isolation *monitor* (LIM) provides that warning. While the isolation *transformer* is invisible to us, the LIM is not. Occasionally the alarm sounds, much to the consternation of the operating room staff. It also has a visible meter and a warning light. The LIM tests each limb of an ungrounded system for a fault to ground. It does so by making contact from one line to ground and measuring the current that flows. Then an analogous contact from the other line to ground is made and the current measured. Figure 7 shows the circuit that exists with the LIM testing the leakage current from line 1. When there is a short from line 1 to the chassis, a complete circuit exists from the transformer via line 1 to the chassis, via the ground*ing* conductor to the LIM test circuit, to line 2 and back to the transformer. Therefore, current will flow and the LIM meter will register it. This current may range anywhere from the small leakage currents due to capacitive coupling to the large flows associated with short circuits owing to direct contact of exposed conductors.

How much current is too much? The National Fire Protection Association (NFPA) guidelines[24] define several different circumstances. The LIM alarm will sound at a collective leakage current of 2 mA. The code sets maximum allowable leakage currents for all patient care areas, whether serviced by isolated power or not: hard-wired devices cannot exceed 5 mA current from chassis to ground*ing* conductor, whereas leakage for devices connected via power cords must be less than 100 μA.[24] When the device is connected to a patient via a lead, maximal leakage currents are more stringent: 50μA for nonisolated inputs and 10 μA for isolated inputs. A patient lead is "any deliberate electrical connection which may carry current between an

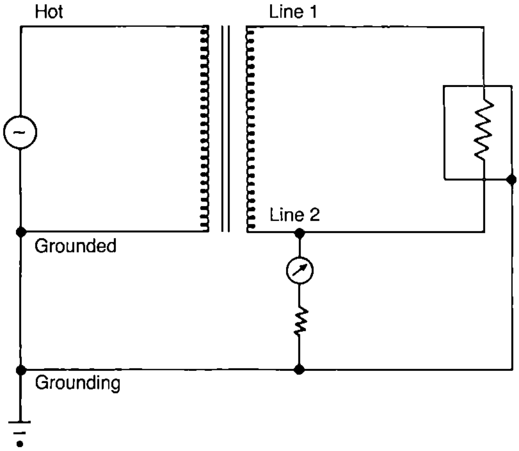


Figure 7. The line isolation monitor test circuit is drawn in as it would appear during testing of line 1 for leakage. Any connection from line 1 to the chassis (or other structure connected to the ground*ing* conductor) can now carry current because the connection from ground*ing* conductor to line 2 has been recreated via the LIM test circuit. The current that would flow in a grounded system is thus measured and displayed so that personnel will be warned of a potential device fault.

appliance and a patient." Examples include ECG electrodes, implanted pacemaker wires, and conductive tubing. An isolated patient lead is one with properties that limit current flow to ground or to the power line to levels that are below hazardous limits.

The line isolation *transformer* converts the grounded system to an ungrounded one, thus allowing a single fault to ground to occur without disabling service. The line isolation *monitor* detects that first fault so that the defective device can be promptly repaired. The isolated power system does *not* warn of potential microshock hazard (2 mA is well over tenfold the current known to cause microshock). It cannot prevent shock resulting from two-conductor contact (gripping line 1 in one hand and line 2 in the other hand). Furthermore, devices without ground*ing* conductors (those with two-prong power cords instead of three-prong cords) cannot return stray currents for detection by the LIM. Use of these devices (most notable portable radios) is hazardous. In fact, NFPA 99 forbids use of two-prong devices in all patent care areas.

The latest NFPA guidelines for health care facilities have removed the requirement for a line isolation transformer and line isolation monitor. Facilities constructed subsequent to 1984 need not have these safety features. Because inclusion of isolated power systems in the operating room and intensive care environments provides additional safety for patients and personnel, anesthesiologists should know whether their particular facilities use isolated power systems. Without isolation, knowledge of circuit breaker location and immediate access to circuit breakers is essential in the event of unexpected power interruption owing to a device that develops a single fault. Hospital planners should be implored to spend the additional funds to provide isolated power to selected environments.

ELECTROCAUTERY

Electrocautery is of interest owing to the possibility of burn at patient attachment.[2,3,13,25] The electrosurgical (ESU) coagulates tissue by heating it. High current density passing via the tip of the ESU wand through tissue provides the thermal energy. Employment of radiofrequencies (5 kHz to 2 MHz) obviates concern for electrocution (Fig. 4). Current fans out from the wand and returns to the ESU device via a return electrode. The return electrode is placed over a muscle mass and contacts the skin through a layer of highly conductive electrode gel. The return plate does *not* constitute an electrical ground. It is neither ground*ed* nor ground*ing*. It is not in contact with the floor or the earth outside. It simply completes the loop for the ESU current.

Current density everywhere besides the tissue directly underneath the tip of the wand is sufficiently low to prevent tissue heating and burn. However, if the normal return path is not available (for example, the electrode pad is not attached to the patient), then current might find an alternate path back to the ESU via a patient lead such as an ECG electrode. The current density through underlying skin may then be great enough to cause tissue heating and burn.[13] Safety is enhanced by using devices (for example, ECG monitors) with isolated patient leads. This additional isolation occurs inside the device and can be achieved with transformers or optical coupling. Modern ESU devices have internal circuitry that disables the device when the return electrode is not attached to the device or if the return electrode wire is broken. ESU devices cannot determine when the electrode is not properly placed on the patient or when the electrode gel has dried, however.

PRINCIPLES OF ELECTRICAL SAFETY

We can assure safety for ourselves and our patients by not defeating the features designed into the operating room electrical system and by following simple guidelines.

1. Devices should be grounded so that unwanted currents return via grounding paths and not via people.
2. People should not be grounded. Rubber-soled shoes are desirable.
3. Devices discovered to be defective by sounding the LIM alarm should be removed and repaired as soon as possible within the dictates of patient safety. For example, it is not appropriate to replace a cardiopulmonary bypass machine during bypass: the electrical hazard from the machine is at most a single fault.
4. Isolate all leads connected to a patient from potential sources of unwanted current.
5. Assure a functioning return path for current when using electrocautery.

CALIBRATION OF MONITORING DEVICES

Measuring the Data

All physiologic data can be displayed in either analog or digital form. Analog data vary on a continuous scale; digital data have discrete values. In the operating room, examples of analog data displays are ECG waveforms, all pressure tracings, and temperatures read from a meter. Examples of digitally displayed data are heart rate, respiratory rate, and systolic/diastolic pressures. All numerical displays are, by definition, displaying digital data.

All physiologic processes are essentially analog in nature. Blood pressure, airway pressure, and velocity of blood flow are all analog data. Some physiologic processes seem to be digital in nature, but they are actually derived from analog data. For instance, the ECG waveform can be interpreted to determine the heart rate; the pressure tracings can be processed to display the systolic, mean, and diastolic pressure; and, the patient's temperature can be displayed as a single number on a cathode-ray tube (CRT) screen.

Similarly, digital data can be converted into analog form. An example is the trending display that exists on many monitors—one can see a graph (analog) of the heart rate or systolic pressures (discrete digital values) of the previous few hours.

Let us examine the steps involved when measuring and processing physiologic signals. First the data must be transduced to an electronic signal. Then the signal needs to be amplified and perhaps filtered. If the signal is to be displayed digitally, it must then be converted into digital form and further processed before being displayed. If the signal is to be displayed in analog form, further processing is usually unnecessary. The transducer that converts the physiologic signal into another signal, the algorithm that is used to convert the data into digital form, and the characteristics of the display device all introduce errors into the signal being measured. These sources of error will be discussed.

Transducing the Data

The first step in measuring physiologic signals is to *transduce* the signal. A transducer is a device that converts one form of energy, such as the pressure in the radial artery, into another form of energy, such as an electrical signal. When transducing pressures using invasive catheters, one must also take into account the characteristics of the pressure tubing system that is used to transmit the pressure from the artery to the transducer. Although the transducers are capable of faithfully reproducing signals with frequencies much higher than those seen clinically, the pressure tubing is not.[5] There are two characteristics of the system that must be examined: the resonant or natural frequency and the damping factor.

The resonant frequency is the frequency at which the system tends to vibrate naturally. It is also the frequency at which the tubing provides the greatest amplification of the pressure wave. In order for the pressure monitoring system to transmit pressure waves accurately, the resonant frequency should be a few times higher than the frequencies present in the pressure wave. For radial artery traces, the highest frequency present is about 20 to 25 cycles per second. The resonant frequency is proportional to the tubing radius, and to the square root of the tubing length, and inversely proportional to the square root of the compliance of the tubing.

The damping coefficient describes the tendency of the system to attenuate or dampen the amplitude of any signal. If the damping coefficient is low (a typical value seen is 0.2), then only pressure waves with frequencies one fifth the resonant frequency or lower will be faithfully reproduced.[7] Higher frequencies will be severely attenuated. An optimal damping coefficient is between 0.6 and 0.7. The damping coefficient is inversely proportional to the tubing radius cubed, and proportional to the square root of the tubing length and the square root of the compliance of the system.[7] Large bore tubing, long lengths of tubing, and air bubbles in the tubing all have a net effect of diminishing the fidelity of the final signal.

After transduction, all signals need to be amplified. In order to reduce the signal-to-noise ratio (that is, the interference from other, unwanted signals), small amplifiers are often packaged with the transducer to amplify the signal before it is sent via electrical cables to the monitor.

This signal is then further amplified and filtered (this will be described later) before being displayed in either digital form (for example, numerical systolic pressure) or in analog form (for example, the arterial pressure trace seen on the oscilloscope). We usually assume that amplifiers do not distort the signal to any great extent. This is probably true for new machines, but not necessarily for old machines. As vacuum tubes in the old amplifiers age, the distortion of the signal increases.

Analog Displays

When it is desirable to observe moment-to-moment variations in a signal, the data are best presented in analog form. Typically, analog data are displayed by using electron beams to graph the data on a phosphor screen (this is what happens on CRT screens or oscilloscopes), by printing the data on a moving piece of paper (chart recorder), or by looking at the placement of a needle on a scale.

Some displays, such as the traces seen on the CRT, have little distortion because an electron beam can be made to follow the fluctuations of any signal with little loss of fidelity in the process. On the other hand, all strip chart recorders, including all hospital ECG machines, introduce distortion. Part of this distortion arises from poor calibration of the instrument. Most of the distortion is due to the fact that the inertia of the writing instrument does not allow it to change direction fast enough to follow the rapid changes in the physiologic signal. The high-frequency components of the signal become damped or attenuated, with the lower frequencies more faithfully reproduced. Fortunately, most of the useful information is located in the lower frequencies.

Filtering

The goal of filtering is to block or attenuate certain frequencies selectively while leaving other (more important) frequencies unchanged. Unfortunately, it is often impossible to eliminate only unwanted frequency components without altering other frequency components.

Filtering the high-frequency components of an arterial pressure trace will rid the waveform of unwanted jaggedness, but the dicrotic notch can be altered or even obliterated if there is too much filtering. Filtering of ECG signals is necessary to produce recognizable signals, but it can cause unrecognized artifact. High-frequency filtering removes muscle and ESU interference. However, it also removes any "notching" that might exist. Sixty cycles per second filtering removes interference due to the power lines and the overhead lighting, but it will also eliminate any component of the ECG signal that is near 60 cycles per second.

Low-frequency filtering (which can be obtained by placing the machine in monitor mode) reduces motion artifact and helps identify the ECG rhythm. However, it also distorts the ST segment and can either cause apparent ST-segment depression or elevation when none exists, or show an isoelectric ST segment when the segment is not isoelectric. Figure 8 shows an example of this phenomenon.

The fidelity of an analog system must be periodically checked. Two aspects must be verified: calibration and frequency response. Calibration is easily accomplished. Most machines that measure ECG

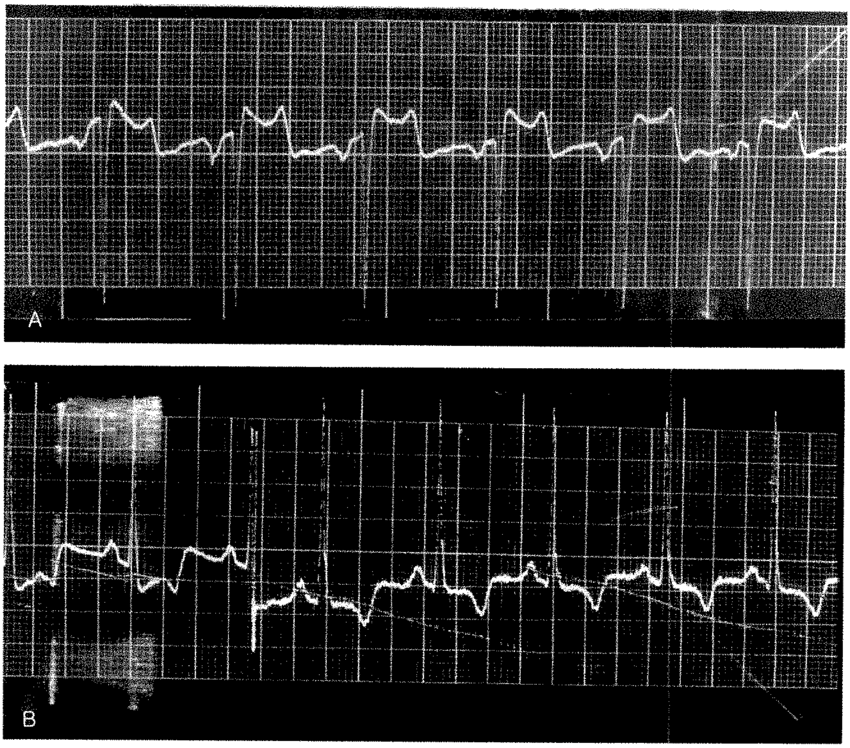


Figure 8. *A*, a strip chart recording of an ECG. The filter switch was set to "monitor" mode. Note the apparent ST-segment depression caused by attenuating the low-frequency components of the ECG signal. The same ECG tracing continues in *B*. After two beats, the filter switch was moved to the "diagnostic" mode, thereby eliminating the low-frequency filter. No ST-segment depression is shown; only the inverted T waves remain.

or pressure can generate a known voltage or pressure. Typical calibration signals are 1 mV for ECGs and 100 mm Hg for pressure channels.

Older pressure measurement systems provide zero and calibration signals. The zero signal is applied first while the zero control is varied to display a zero output. For this maneuver, the pressure measurement system is exposed to atmospheric pressure at a desired height, usually the level of the atrial chambers of the patient's heart. After zeroing, the calibration signal is applied and the gain control adjusted to provide an output equal to the value of the calibration signal. Newer pressure measurement systems require zero adjustment only. Elimination of routine pressure transducer calibration is afforded by improvements in transducer design, manufacturing, and quality control.

The frequency response is more difficult to check. The best approach is to provide a series of different inputs to the machine. Each input is of constant amplitude, but of different frequency. Ideally, the output of the machine should also be of constant amplitude ("flat response") and at the same frequency as each of the inputs. Great care is taken to assure a flat response in high-fidelity sound systems. In the operating rooms, this means of determining the frequency response is cumbersome and impractical.

A simpler, and more clinically useful technique has been described by Gardner.[16] In Gardner's method, an impulse signal is applied to the pressure monitoring system. This can be accomplished by giving a quick flush to the tubing catheter system. The resulting pressure transient is plotted on a chart recorder. From the plot, the natural frequency and the damping coefficient can be determined. By independently varying the natural frequency and the damping coefficient, Gardner showed that the higher the natural frequency, the lower the damping coefficient can be before noticeable distortion of the waveform occurs. Interestingly, introducing an air bubble into the pressure tubing (a common practice used to reduce the "overshoot") is ill-advised because while this increases the damping coefficient (good), it also lowers the resonant frequency (bad).[9] Best results are obtained by eliminating all air bubbles from the catheter systems and by using short, low-compliance tubing without injection ports.

Digital Displays

Most of the newer monitoring devices present their data in digital form, even though the data are usually analog in nature. Consequently, there needs to be some algorithm or technique by which the analog data is converted into digital form. This process of analog to digital (A to D) conversion causes a small amount of error to be introduced because the once continuously variable signal is now represented by a series of data with discrete values.

The processing of digital data can be more complicated than the processing of analog data because there are many different algorithms that can be used to analyze the data. The algorithm determines the accuracy of the output. Unfortunately, no one algorithm works perfectly for each application all the time. The following discussion focuses on some of the general principles behind the many algorithms in use today. First the digital algorithms used to process QRS data are examined; then the algorithms used to process pressure data are examined.

Electrocardiogram Processing

The first step of ECG processing is to determine the heart rate by measuring the R-R interval. The peak of a single QRS wave (that is, the peak of the R wave) is first located by looking for the point where the signal is not only at a maximum, but also where the derivative of the signal (that is, the slope of the ECG trace) changes from positive to negative. Needless to say, a good algorithm will not be confused by tall, peaked P or T waves; an rR′ configuration to the QRS; ESU interference; or any of the many dysrhythmias.

Once the R wave has been found for each of the QRS complexes, and the time between each R wave measured, a simple calculation will produce the heart rate:

$$\text{Heart rate} = 60/\text{R-R interval in seconds}$$

Of course, most of us would be displeased if the algorithm did not also average the R-R intervals so as to eliminate some of the artifactual beat-to-beat variation that exists in the signal. Unfortunately, this averaging will also eliminate some of the physiologic beat-to-beat variation. Figure 9 shows the effect of averaging three R-R intervals together before displaying the heart rate. The plotted data is listed in Table 1. As can be seen, there is less fluctuation in the averaged data than in the original data. Inspection of Table 1 reveals that while the original data varies from 58 to 64, the displayed value varies from 59 to 63.

The next step is to separate the ECG signal into the various com-

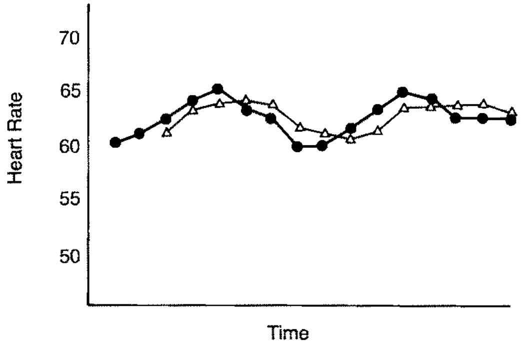


Figure 9. An example of three point averaging. The open circles represent the heart rate determined from sequential R-R intervals in a hypothetical patient. The open triangles represent the heart rate determined by averaging the three most recently determined rates in the same hypothetical patient. The averaged points are the output of a very crude low-pass filter that filters the high-frequency components present in the original signal. These high-frequency components are represented by the beat-to-beat variation in the data.

Table 1. *Example of Three-Point Digital Filter*

HR	FILTER VALUE	DISPLAY VALUE
60	—	—
60	—	—
61	60.3	60
62	61.0	61
64	62.3	62
63	63.0	63
60	62.3	62
58	60.3	60
60	59.3	59
61	59.7	60
62	61.0	61
64	62.3	62
64	63.3	63
62	63.3	63
61	62.3	62

ponent parts (P wave, QRS, ST segment, T wave, etc.). This processing is much more complicated. The ST segment, because it can take many morphologies, is particularly difficult to define. Many algorithms define the ST segment as the segment of the waveform that begins a certain number of milliseconds after the J point (often 80 ms), and ends when the ECG signal returns to baseline.

Because there is inherent noise in all ECG signals, the ECG signal is usually preprocessed by passing it through a high frequency (low-pass) filter before significant analysis of the signal begins. This preprocessing can either be done with analog circuitry (equivalent to passing the signal through a resistor and capacitor network) or by digitally filtering the signal. Averaging the last few data points, as was done in the example shown in Table 1 and Figure 9, is but one (crude) example of a digital low-pass filter. Algorithms used to process ECGs can be fairly complex.[15] Only the basic concepts have been presented here.

Pressure Measurement

Noninvasive blood pressure measurements are often accomplished using auscultatory techniques. Automated blood pressure machines, such as the DINAMAP machine (Criticon, Inc., FL) determine systolic, mean, and diastolic pressures using an oscillotonometric technique.[12]

Invasive blood pressure measurement techniques involve more complicated processing. Consider mean arterial pressure first. The easiest method of obtaining a mean arterial blood pressure from an arterial trace is to pass the signal through a resistance/capacitance network designed to act as a low-pass filter allowing passage of only very low frequency signals (for example, 0.2 Hz or lower). Essentially, this circuit acts to average the signal, thereby giving the mean. For example, setting the display switch to the "filter" position on an E for

M monitor (Honeywell) causes the mean pressure to be displayed on the screen because of the insertion of a low-pass filter. Digitally, this can be accomplished by averaging the signal for the last few seconds. The longer the averaging period, the more filtering of the higher frequencies (the lower the "bandwidth"), and the less variation in the trace. Table 2 lists some typical bandwidths used.[10]

The basic principle behind finding the systolic (or diastolic) pressure from a pressure trace is similar to that of locating the R wave in the ECG signal. The systolic (or diastolic) pressure is found at a local maximum (or minimum) pressure where the slope of the pressure tracing changes sign. If one is simultaneously processing the ECG data, one can use the timing of the QRS to help locate the true systolic pressure generated by each QRS.

As with heart rate, if each systolic (or diastolic) pressure were plotted, there would be a great deal of beat-to-beat variation. In the case of central venous and pulmonary pressures, this variation is artifactual when caused by spontaneous or positive-pressure ventilation.[22] Many anesthesiologists look for the highest pressure displayed if the patient is breathing spontaneously, and the lower pressure displayed if the patient is being ventilated by positive-pressure ventilation. Neither of these methods is entirely satisfactory.[4,11]

Usually, most machines filter the systolic signal using both a high-pass filter to omit the low-frequency respiratory component and a low-pass filter to reduce the noise in the signal. A low-pass filter, such as the one previously described to filter the heart rate, can be used. However, a better digital filter is one in which the most recently measured data is weighted more heavily than the data obtained a few milliseconds prior. There are many examples of such filters. Figure 10 shows a hypothetical pressure wave that has been placed through two different digital filters. The first filter is the average of the latest five

Table 2. *Filter Characteristics for Mean Pressure Measurement Used in Bedside Monitors*

MANUFACTURER	BANDWIDTH* (HZ)	NO. OF POLES†
LDH Hospital	0.08	1
Hewlett-Packard	0.16	2
Tektronix/Vitatek	0.03	4
Mennen	0.12	2
Spacelabs	0.11	2
E for M/Honeywell	0.16	1
Datamedix	0.09	2

*Bandwidth = frequency above which the signal is reduced by 0.707 of the DC amplitude.

†Poles = measure of how quickly the signal is attenuated as the frequency is increased.

From Cengiz M, Crapo RO, Gardner RM: The effect of ventilation on the accuracy of pulmonary artery and wedge pressure measurements. Crit Care Med 11:502–507, 1983; with permission.

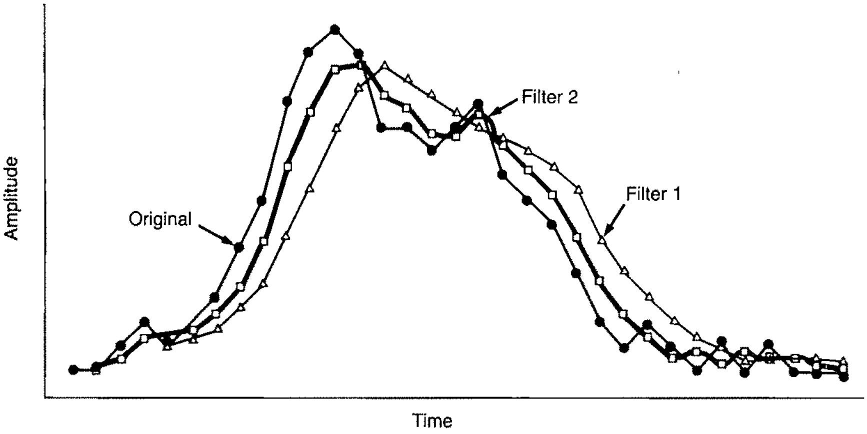


Figure 10. The result of digital filtering of a hypothetical waveform. The open circles represent the original unfiltered hypothetical waveform. The open triangles represent filter 1, a crude low-pass filter. The displayed values are the average of the five previous unfiltered values. Note that the output of this filter is missing the high-frequency components (that is, the "jaggedness") seen in the original signal. The open squares represent filter 2, a better low-pass filter that retains more high-frequency components of the original waveform than filter 1, but still eliminates much of the rapid variations seen in the original signal. This filter is an exponential filter, which is formed by averaging the latest measured (unfiltered) value with the previously displayed (filtered) value.

data points. The second filter is an exponential filter, where each plotted point is the average of the previously plotted point and the current data point. The raw data used to generate Figure 10 is listed in Table 3.

Figure 11 and Table 4 show how these filters process a square wave input. It is easy to see that both filters not only smooth the data, but also cause a delay in the location of the peaks. This delay, called a phase shift, is different for each frequency of the signal.

In the Marquette monitor, a modified exponential filter is used where the weighting of the previous and current samples is dependent on the difference between the two values (personal communication from Marquette Electronics, Inc., Milwaukee, WI). This method of filtering has been shown to emphasize the end-tidal readings, when there is less respiratory-induced fluctuation in the pressures.[14]

Recently, Mitchell et al[23] have described a rather elegant method of processing pulmonary artery pressure. They pass the pulmonary artery pressure signal, in digital form, through a low-pass filter. The output of this filter is essentially the respiratory component of the pulmonary artery pressure. This filtered signal is then subtracted from the original signal to obtain a pressure trace that is devoid of a respiratory component. Algorithms similar to those described previously are used to determine the systolic, diastolic, and mean pressures, which can now be determined more precisely because the influence of ventilation has been eliminated. The data is converted back into analog form and displayed on an oscilloscope (CRT).

Table 3. *Hypothetical Waveform Data Applied to Two Digital Filters*

WAVE	FILTER 1	FILTER 2
1	—	—
1	—	1.0
2	—	1.5
3	—	2.3
2	1.8	2.1
3	2.2	2.6
4	2.8	3.3
6	3.6	4.6
8	4.6	6.3
12	6.6	9.2
14	8.8	11.6
15	11.0	13.3
14	12.6	13.6
11	13.2	12.3
11	13.0	11.7
10	12.2	10.8
11	11.4	10.9
12	11.0	11.5
9	10.6	10.2
8	10.0	9.1
7	9.4	8.1
5	8.2	6.5
3	6.4	4.8
2	5.0	3.4
3	4.0	3.2
2	3.0	2.6
1	2.2	1.8
2	2.0	1.9
1	1.8	1.4
2	1.6	1.7
1	1.4	1.4
1	1.4	1.2
1	1.2	1.1

SUMMARY

The fidelity of all monitored data is influenced by the characteristics of the transducer system. In the case of invasive catheters, the tubing used and any air bubbles in the tubing have a great influence on the values displayed on the screen. Low compliant tubing and absence of air bubbles keep the natural frequency and the damping coefficients high, and are essential to accurate output.

The fidelity of analog displays is also limited by the frequency response and the damping characteristics of the writing instrument used. An instrument with little mass (low inertia) will be able to follow rapidly moving signals without damping the high frequencies present in the signal. The amplifier used to amplify the signals produced by the transducer must also be of high quality.

Digitally processed signals are plagued with calibration problems, too. All digital filters, just like analog filters, introduce phase

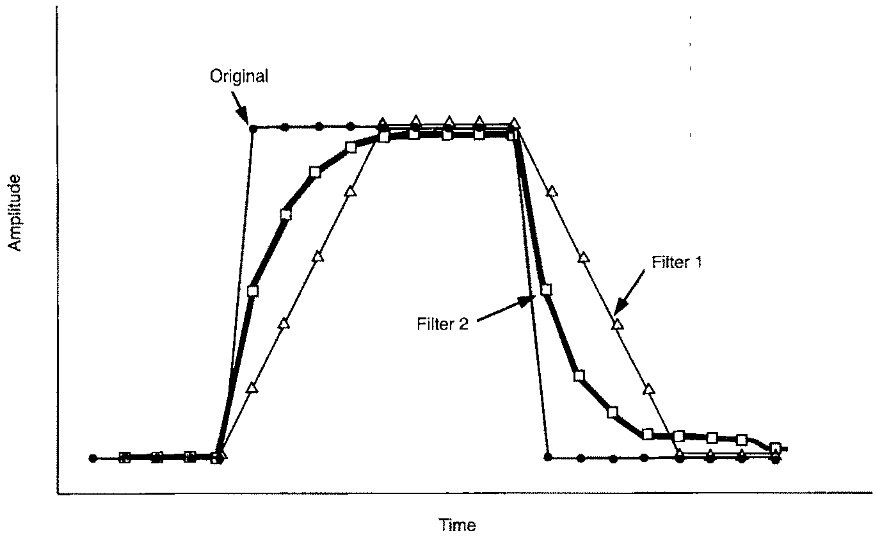


Figure 11. Square wave filtering. The open circles represent the square wave input to a digital filter. The open triangles represent filter 1, a crude low-pass filter. The filter output (displayed value) is the average of the previous five measured values. This filter attenuates high-frequency components. The open squares represent filter 2, a better low-pass filter to reduce high-frequency noise. The output (displayed value) of this filter equals the average of the current measured value and the previous displayed value. This is an example of an exponential filter.

Table 4. *Square Wave Data Applied to Two Digital Filters*

WAVE	FILTER 1	FILTER 2
0	—	—
0	—	0.0
0	—	0.0
0	—	0.0
0	0.0	0.0
10	2.0	5.0
10	4.0	7.5
10	6.0	8.8
10	8.0	9.4
10	10.0	9.7
10	10.0	9.8
10	10.0	9.9
10	10.0	10.0
10	10.0	10.0
0	8.0	5.0
0	6.0	2.5
0	4.0	1.2
0	2.0	0.6
0	0.0	0.3
0	0.0	0.2
0	0.0	0.1
0	0.0	0.0

shifts into the signal. These shifts are different for each frequency, and they will distort the physiologic signal, which contains many frequency components. Even more important, digitally analyzed signals use many complex algorithms to separate noise from signal, and to decompose each signal into its important segments (systolic, diastolic, mean pressures, P wave, QRS, ST segment). These algorithms are not perfect, and, in certain circumstances, can cause erroneous numbers to appear on the monitors.

REFERENCES

1. Atkin DH, Orkin LR: Electrocution in the operating room. Anesthesiology 38:181–183, 1973
2. Aronow S, Bruner JMR: Electrosurgery. Anesthesiology 42:525–526, 1975
3. Becker CM, Malhotra IV, Hedley-Whyte J: The distribution of radiofrequency current and burns. Anesthesiology 38:106–122, 1973
4. Berryhill RE, Benumof JL, Rauscher LA: Pulmonary vascular pressure reading at the end of exhalation. Anesthesiology 49:365–368, 1978
5. Blitt CD: Monitoring in Anesthesia and Critical Care Medicine. New York, Churchill Livingstone, 1985
6. Bruner JMR: Fundamental concepts of electrical safety. Refresher Courses in Anesthesiology 2:11–25, 1974
7. Bruner JMR: Handbook of blood pressure monitoring. Massachusetts, PSG Publishing Company, Inc., 1978
8. Bruner JMR: Hazards of electrical apparatus. Anesthesiology 28:396–425, 1967
9. Bruner JMR, Krenis LJ, Kunsman JM, et al: Comparison of direct and indirect methods of measuring arterial blood pressure, part I. Med Instrum 15:11–21, 1981
10. Cengiz M, Crapo RO, Gardner RM: The effect of ventilation on the accuracy of pulmonary artery and wedge pressure measurements. Crit Care Med 11:502–507, 1983
11. Civetta JM: Measurements in assessing circulatory function. Refresher Courses in Anesthesiology 3:73–80, 1975
12. Dinamap™ Adult/Pediatric and Neonatal Vital Signs Monitor Models 1846 SX and 1846 SX/P Operation Manual. Tampa, Florida, Criticon, Inc. 1986
13. Finlay B, Couchie D, Boyce L, et al: Electrosurgery burns resulting from use of miniature ECG electrodes. Anesthesiology 41:263–269, 1974
14. Fish DJ, Teplick R: Clinical value of variable weight filter algorithm equipped monitors for invasive pressure measurement (abstract). Anesthesiology 65:A156, 1986
15. Forbes AD, Jimison HB: A QRS detection algorithm. J Clin Monit 3:53–63, 1987
16. Gardner RM: Direct blood pressure measurement—Dynamic response requirements. Anesthesiology 54:227–236, 1981
17. Geddes LA, Baker LE: Response to passage of electric current through the body. J Assoc Advance Med Instrum 5:13–18, 1971
18. Graystone P, Towell ME: Electric shock hazard associated with pressure transducers. Anesthesiology 34:79–80, 1971
19. Hopps JA: Shock hazards in operating rooms and patient-care areas. Anesthesiology 31:142–155, 1969
20. Leeming MN: Protection of the "electrically susceptible patient." Anesthesiology 38:370–383, 1973
21. Leonard PF: Characteristics of electrical hazards. Anesth Analg 51:797–809, 1972
22. Maran AG: Variables in pulmonary capillary wedge pressure: Variation with intrathoracic pressure, graphic and digital recorders. Crit Care Med 8:102–105, 1980

23. Mitchell MM, Meathe EA, Jones BR, et al: Accurate, automated, continuously displayed pulmonary artery pressure measurement. Anesthesiology 67:294–300, 1987
24. National Fire Protection Association: NFPA 99 Standard for Health Care Facilities. Quincy, MA, 1984, pp 99–13
25. Neufeld GR: Principles and hazards of electrosurgery including laparoscopy. Surg Gynecol Obstet 147:705–710, 1978
26. Richter HP, Schwan WC: Wiring simplified, ed 35. St. Paul, Park Publishing, Inc., 1986, pp 47–56

Department of Anesthesiology
Hahnemann University
Broad and Vine Streets
Philadelphia, PA 19102-1192

0889–8537/88 $0.00 + .20

Noninvasive Blood Pressure Measurement

Theodore Jay Sanford, Jr, MD, Brian R. Jones, MD,† and N. Ty Smith, MD‡*

Increasingly bold surgery, increasingly ill patients, and recently established standard of care guidelines have increased the need for simple, accurate, and robust blood pressure monitoring devices. However, invasive blood pressure monitoring has potential cardiovascular complications, is not easily portable, and cannot be used for prolonged periods. Since Cushing's initial attempts to bring blood pressure recording into the operating room, noninvasive monitoring of blood pressure has been slowly accepted. Recording blood pressure is considered essential now, and a recent review listed over 80 suppliers of noninvasive blood pressure measuring devices.[43] These systems include the classic manually operated cuff and stethoscope, as well as automated systems that measure systemic blood pressure either intermittently or continuously. Understanding the principles of each noninvasive monitoring modality will aid the practitioner in making informed purchasing and clinical decisions.

Currently, the noninvasive measurement of blood pressure is accomplished by either occlusive or nonocclusive devices. The occlusive devices use an air-filled cuff placed around an arm, leg, finger, or toe. Inflation of the cuff occludes an artery, and as the air is released from the cuff, return of the arterial pulse is detected and analyzed by various methods to determine systemic blood pressure. These methods include auscultation, oscillometry, palpation, ultrasound, and flush, or return to flow. Nonocclusive measurements also use air-filled cuffs but do not rely on obliteration of the pulse. Methods of analysis used by nonocclusive methods include the Penaz method and a computer model of arterial wall displacement.

University of California San Diego and Veterans Administration Medical Center, San Diego, California

*Associate Clinical Professor of Anesthesiology
†Chief Resident in Anesthesiology
‡Professor of Anesthesiology

This article focuses on the principles of blood pressure measurement. These principles can be classified as occlusive versus nonocclusive, intermittent versus continuous, or manual versus automated. These classes are not mutually exclusive, and we shall describe manual intermittent, automated intermittent, and nonocclusive continuous systems.

OCCLUSIVE METHODS

Most of the widely used methods of noninvasive blood pressure measurement entail occluding an artery and then noting the return of a signal upon the release of pressure from a cuff. Arterial occlusion methods differ mainly in the way they detect the reappearance of this signal. The choice of the detecting method has widely varying clinical implications, including the ease of application, the accuracy, the speed of a measurement, and the response to artifacts. Because of the temporary obliteration of the pulse, pressure measurement can be made only intermittently, and there is little information about the waveform.

The occlusive methods used singly or in combination are (1) auscultation of Korotkoff sounds, (2) oscillation, and (3) detection of blood flow distal to the sphygmomanometer cuff by palpation of a pulse, Doppler ultrasound, or photoelectric plethysmography. This section reviews the physiology, as well as the advantages and disadvantages of these methods.

Auscultation

Auscultating the appearance and disappearance of Korotkoff sounds is the most common mode of manual noninvasive blood pressure measurement. Classically, Korotkoff sounds have been divided into five phases: phase I, "a loud, clear-cut snapping tone"; phase II, "a succession of murmurs"; phase III, "the disappearance of murmurs and the appearance of a tone resembling to a degree the first phase but less marked"; phase IV, "the tone becomes less clear in quality or dull (muffling)"; and phase V, "the disappearance of all sounds."[1] Although the mechanism producing Korotkoff sounds has not yet been established, turbulent flow, a water-hammer effect, arterial flutter, amplification of perturbations of a dynamically unstable artery, and other explanations have been suggested.[8,54]

An occluding cuff is placed on an extremity, usually the upper arm, and a stethoscope is placed over the previously palpated brachial artery. The cuff is inflated until the pulse is obliterated, and the pressure in the cuff is slowly released. Systolic pressure is recorded when the first snapping sounds are heard. As the cuff continues to deflate, the sounds disappear and then return again before the diastolic muffling. This silent interval, the so-called auscultatory gap, is of unknown etiology and must be considered; otherwise an underestimation of systolic or overestimation of diastolic pressure may occur.

Systolic pressure is thought to occur with the onset of phase I sounds. Currently, most investigators agree that the diastolic pressure occurs with the onset of phase V (disappearance of all sounds). The American Heart Association (AHA) has recently recommended that the diastolic pressure be reported with the onset of phase IV in children and phase V in adults.[1] Phase IV values overestimate intra-arterial diastolic pressure by 5 to 10 mm Hg, whereas complete loss of Korotkoff sounds closely approximates true diastolic pressure but is subject to larger random errors.

In clinical practice, the auscultation method remains the standard manual method because of its relative immunity to artifacts and accuracy over a wide range of pressures. Auscultation correlates well with intra-arterial measurement, but only systolic and diastolic pressure can be measured.

Automated Auscultatory Systems

There are several automated auscultatory blood pressure monitors currently available. In these systems the occlusive cuff is filled to a prescribed pressure and then released at a set rate or in steps.[13] During cuff deflation, a microphone under the cuff transduces Korotkoff sounds and the amplitude and frequency of the sounds are processed to determine systolic and diastolic pressures. The step method has the advantage of comparing several cardiac cycles at each pressure-step, a maneuver that improves the accuracy. The disadvantage is that the determination time is increased. Initial sensitivity to the correct placement of the microphone directly over the artery has been overcome with newer microphones and better computer algorithms.

The accuracy of either manual or automated auscultatory methods depends on cuff size, accuracy of aneroid manometer, location of the stethoscope, and user ability to hear, see, and feel. A cuff that is too small or loosely applied will give artificially high readings.[6] The AHA recommends a cuff-bladder width of 13 cm for a standard size adult, or 20 per cent greater than the diameter of the arm.[1] The bladder should cover at least half of the circumference of the extremity with the middle of the bladder positioned over the pulsating artery. The manometer itself can cause inaccuracies. Perlman evaluated 310 hospital aneroid sphygmomanometers and found 13.2 per cent had average deviations greater than 7 mm Hg.[38] The regular calibration of the aneroid manometer against a mercury manometer can decrease inaccuracies. Finally, the location of the stethoscope is more important than the type of stethoscope. It is worth the effort to secure the stethoscope over the brachial artery to maximize the ability to hear Korotkoff sounds.

Auscultation is least reliable at low pressures.[39] In addition, some flow actually occurs before sufficient energy is generated to create a sound; therefore, a lower value than simultaneous intra-arterial measurement occurs.[15] Accuracy is also related to heart rate and cuff deflation rate. The faster the rate of deflation, the greater the decrement in cuff pressure between heart beats, and the more widely the recorded value may vary from the actual point at which the flow pattern changes. Similarly, at a given cuff deflation rate, the heart rate is inversely related to the accuracy of the measurement. With a slow heart rate, the manometer will fall further between beats leading to less sensitivity.[43] The AHA recommends a pressure release of 2 to 3 mm Hg per heart beat.[1]

Comparison of the accuracy of indirect auscultatory reading with direct arterial pressure and reasons for inaccuracy have been reported. Discrepancies between direct and indirect pressure are created from normal cardiovascular physiology; for example, at the site of the direct and indirect measurements, systolic blood pressure is higher toward the periphery than in the aortic arch.[55] Van Bergen observed that compression of the brachial artery immediately distal to the intraarterial catheter resulted in a 20 to 30 mm Hg elevation of direct systolic pressures measured by cuff. This was thought to be an example of reflection in the periphery causing amplification of the waveform. If direct intra-arterial pressures are measured in one arm and indirect pressures measured in the other, the potential for measurement differences arising from normal physiologic variations in each arm arises. Goldhill measured bilateral simultaneous indirect blood pressure in patients and found 37 per cent of patients had a difference in pressure between arms equal to or greater than 6 mm Hg and 13 per cent had differences of 11 mm Hg or more.[20]

The physical characteristics of the external monitoring system can also influence the comparison of direct and indirect measurements. The accuracy of direct arterial measurements, the "gold standard," has been questioned because of different frequency response and dampening of the recording systems.[5] Adequate response is dependent on the catheter, connecting tubing, and transducer setup. Comparing the results from one study with those of another can be difficult because of different characteristics of measurement systems and data analysis.

To compensate for the occasional inability to hear Korotkoff sounds, a system has been introduced (IVAC 560, IVAC, San Diego, CA) that uses auscultation for most determinations yet defaults to oscillometry when auscultation fails (Table 1). Using this device in 50 patients, Davis reported that auscultatory and oscillometric values closely correlated with each other.[9] However, both indirect methods underestimated systolic and overestimated diastolic pressures when compared with radial artery values.

Infrasound

The majority of sound energy in Korotkoff sounds occurs in the subaudible range, known as infrasound. This subaudible sound energy can be electronically detected to provide another means of blood pressure determination. In certain clinical situations, for example, hy-

Table 1. *Representative Blood Pressure Devices*

DEVICES	MANUFACTURER
Occlusive	
Auscultation	
Infrasounde D4000	Puritan-Bennett Corp.
Oscillometric	
Dinamap 1846	Critikon, Inc.
Omega 1000	Invivo Research Labs Inc.
Accutorr I	Datascope Corp.
Air-shields adult	Air-shields
Ohmeda NIBP	BOC Healthcare
Combined auscultation and oscillometric	
Vital-Check 4000	IVAC Corp.
Kendall 8200	Kendall Co Hospital Products Division
Paramed 9200	Paramed Technology Inc.
Doppler wall movement	
Arteriosonde	Roche Medical Electronics Inc.*
Nonocclusive	
Penaz method	
Finapres 2300	BOC Healthcare
Computerized wall displacement	
Cortronics APM 770	Cortronic Corp.

*No longer available.

potension or arteriosclerosis, standard Korotkoff auscultation can be impossible or inaccurate.[53,58] Yet with electronic amplification and interpretation of the low frequency sounds, the blood pressure can frequently be determined.

One automated infrasound devide, the Infrasounde D4000 (Puritan-Bennett Corp.), is currently available. This device uses wide-range microphones to pick up the low frequency signals, less than 30 Hz, and then electronically determines systolic and diastolic pressures. Nystrom et al[36] compared intra-arterial radial artery pressures with readings from this device and a common oscillometric device (Dinamap). For both the Infrasounde and the oscillometric system the difference from the direct pressure averaged from 8 to 14 mm Hg for both systolic and diastolic blood pressures. The average Infrasounde systolic pressure was 13.3 mm Hg lower than the intra-arterial, and the Infrasounde diastolic pressure was 4.7 mm Hg higher than the intra-arterial. Differences were thought to be due to the normal physiologic variations between patients and also to the time lag between direct and indirect pressure measurements on the same extremity.

Oscillometry

Blood pressure determination by oscillometry was used before the auscultatory method was reported.[17] The simplest systems use an occlusive cuff, and blood pressures are inferred from observations of oscillations of the needle indicator of a connected manometer. Following inflation of the cuff to a point where the pulse disappears, the pressure in the cuff is released and oscillations of the indicator needle are noted. In manual systems systolic pressure is assumed to occur at the point where the oscillations suddenly increase, and diastolic pressure is noted at the point where the oscillations first become slurred or disappear. The mean blood pressure is thought to be the point of largest oscillation. Again, as with Korotkoff sounds, the point of diastolic pressure is controversial and is not universally agreed upon.

A special oscillometric apparatus, the von Recklinghausen system was designed to magnify the cuff-pressure oscillations. The system uses a wide cuff containing two interconnected narrow inflatable bladders. Both bladders are inflated above systolic pressure and then slowly deflated. When systolic pressure is reached, blood flow beneath the upper cuff strikes the lower cuff and creates a pressure wave that is transmitted to the manometer. Each pulse wave creates an oscillation of the mercury column or aneroid needle. Hutton and Prys-Roberts[27] recently reviewed a commercial manual oscillometric system with interconnected bladders and drew three conclusions: (1) For detection of systolic pressures the first change in character of the needle oscillations should be used; (2) the mean pressure corresponded with the maximum oscillations; and (3) the diastolic determination was essentially impossible.[27]

Advantages of the oscillometric method include the ability to determine values at low levels of arterial blood pressure and no requirement for a stethoscope or other method of peripheral pulse detection. Its main disadvantages are that it is prone to artifacts from patient movement and can be incapacitated by dysrhythmias.

Automated Oscillometric Devices

Automated oscillometric systems differ from simple manual systems in that oscillations are electronically measured and amplified. Algorithms are used to determine systolic, diastolic, and mean pressures. The first automatic oscillometric device introduced measured only the mean arterial pressure and was labeled DINAMAP (*D*evice for *I*ndirect *N*oninvasive *A*utomated *M*ean *A*rterial *P*ressure) (Fig. 1).[42] At the time many argued that the mean pressure was the only pressure needed, and with the oscillometric devices this was the easiest value to determine (Fig. 2).

There are several standard features of automated oscillometric devices. Most devices have fairly reliable artifact detection systems, which either cease cuff deflation until movement has stopped or terminate the present determination if the movement persists beyond a preset time interval. In addition, most systems have multiple interchangeable cuffs. Many automated systems measure the volume of air required to fill the cuff and can determine if an infant or child cuff is attached by noting the small volume for inflation. A small cuff inflates to a lower starting pressure, approximately 130 mm Hg, instead of the 160 to 170 mm Hg for the adult-size cuff. With subsequent readings the cuff is inflated to approximately 35 mm Hg higher than the previously recorded systolic pressure.

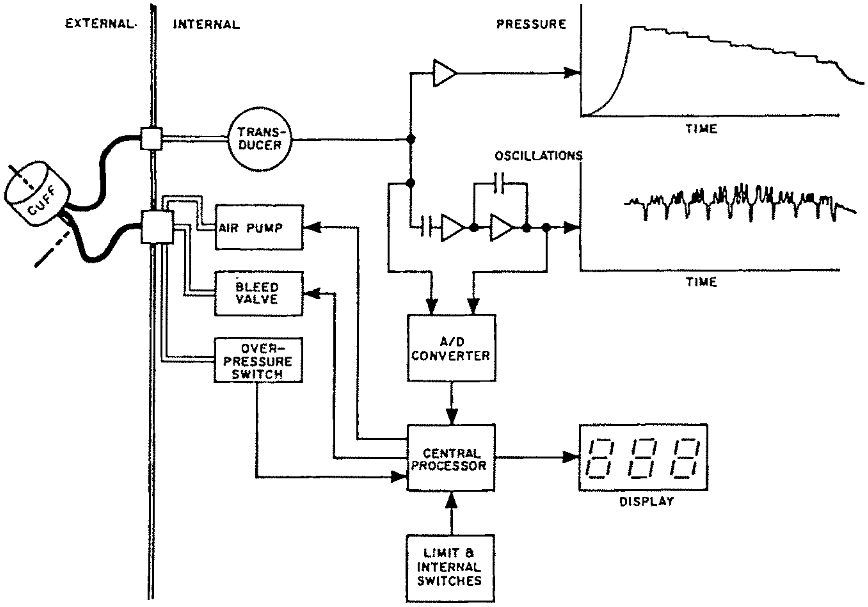


Figure 1. Schematic of major components of the DINAMAP. In the upper right-hand corner of the figure are shown schematically the waveforms that result during a single determination. (*From* Ramsey M: Noninvasive automatic determination of mean arterial pressure. Med Biol Eng Comput 17:11–18, 1979; with permission.)

When automated oscillometric devices were first introduced, many anesthesiologists routinely placed a second blood pressure cuff on the arm opposite the automatic side as a fail-safe monitor. Riopelle addressed this concern by modifying a standard DINAMAP to allow simultaneous auscultatory and oscillometric determinations by adding an aneroid manometer and hand-pump.[44] This modification also allows calibration of the digital pressure readouts.

Accuracy of Oscillometry

Clinical studies have reported varying correlation between direct and oscillometric blood pressure determinations. Hutton evaluated the DINAMAP with direct intra-arterial pressure in ten patients and found systolic, diastolic, and mean correlation coefficients to be 0.95, 0.85, and 0.87, respectively.[28] Systolic and mean pressure were underestimated at high intra-arterial pressures and overestimated at low intraarterial pressures. The diastolic pressure measured by DINAMAP was consistently higher than intra-arterial values.

An early study by Yelderman and Ream[61] compared the oscillometric technique with direct arterial mean pressure in the contralateral radial artery in 19 patients. He reported that the pooled data had an average error of 1.4 mm Hg, while the error for any single determination was up to 14 mm Hg. Rutten et al[46] compared mean arterial pressure from five different automatic oscillometric blood pressure

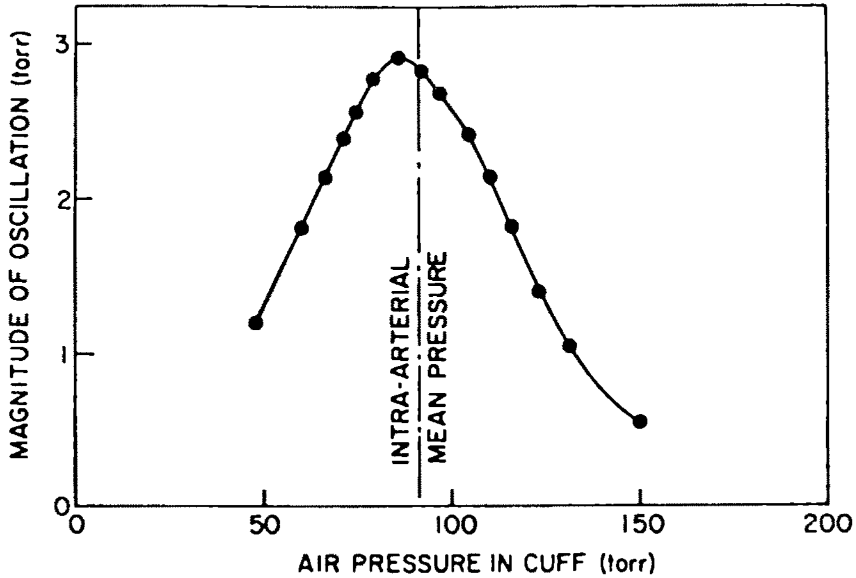


Figure 2. An average of several values of mean arterial pressure determined by the oscillometric technique. The amplitude of oscillation of cuff pressure is plotted against cuff pressure. True mean arterial pressure is shown for comparison. (*From* Yelderman M, Ream AK: Indirect measurement of mean blood pressure in the anesthetized patient. Anesthesiology 50:253–256, 1979; with permission.)

monitors with intra-arterial mean pressures and observed that all performed similarly, with a wide range of variation (+40 to −29 per cent) when compared with directly measured mean arterial pressure. There was a tendency to overestimate mean aterial pressure at low values and underestimate mean pressure at high values.

As with auscultatory measurements, the cuff location affects the pressure obtained. Goldthorp compared DINAMAP arm and thigh pressure measurements in 30 patients and found that with appropriate size cuffs, systolic pressures in the thigh were 10 to 40 mm Hg higher than in the arm but diastolic pressures were essentially the same.[21]

Relying on oscillometric measurements during hypotension may be hazardous. Gourdeau et al[22] compared oscillometry with radial arterial pressures from the contralateral arm in 21 patients undergoing deliberate hypotension. They reported correlation coefficients for systolic of 0.94, mean 0.93, and diastolic 0.88, but with large interindividual variability. They also found that the oscillometric methods underestimated blood pressure when intra-arterial pressure was greater than 80 mm Hg and overestimated blood pressure when intra-arterial blood pressure was less than 80 mm Hg. They concluded that an oscillometric system could not replace intra-arterial monitoring in the setting of controlled hypotension because it gave falsely high values during the hypotensive period.[23] Gloyna et al[19] studied the accuracy when the mean intra-arterial pressure was less than 65 mm Hg in ten patients and recorded 280 measurements. The indirect values were higher than intra-arterial by an average of 12.7 mm Hg for systolic, 5.7 mm Hg for diastolic, and 8.8 mm Hg for mean pressures.

Many investigators have reported that automated oscillometric blood pressure devices underestimate blood pressure in hypertensive patients.[32,48] Loubser[32] studied this in 30 hypertensive postcarotid endarterectomy patients and collected 558 readings for systolic, diastolic, and mean pressures. He found the DINAMAP 1845 underestimated diastolic and mean pressures by 6.3 mm Hg and 0.3 mm Hg, respectively. The differences were most pronounced at blood pressures greater than 160 mm Hg, where indirect systolic pressures were underestimated by a range from 20.0 to 53.3 mm Hg less. On the other hand, when the intra-arterial values were less than 160 mm Hg the underestimation was from −0.8 to 12.6 mm Hg.

Oscillometry has been touted as advantageous in infants, in whom auscultation of Korotkoff sounds can be difficult. Friesen evaluated the DINAMAP in 20 patients with ages ranging from 1 day to 2 weeks and weights from 680 to 6000 g.[16] Direct arterial pressures were compared with the DINAMAP, and the correlation coefficients were 0.96 for systolic and 0.94 for diastolic blood pressure.

Peripheral Pulse Detection

The third occlusive method used to measure blood pressure involves detecting the return of the distal pulse by palpation, ultrasound, or plethysmography. Palpation was the method used by Riva-Rocci and is probably the simplest. A cuff occludes the brachial artery, and when the palpated pulse returns, the pressure in the cuff is recorded as systolic pressure and when the pulse is felt to be at its fullest, that is, equal to the strength before cuff inflation, this is diastolic. With this method it is not possible to determine mean arterial pressure, and the diastolic pressure is frequently inaccurate.

The ultrasonic method of pulse detection is based on a principle first described in 1842 by Christian Doppler. Its application entails applying a cuff to occlude a proximal artery. A Doppler transducer placed distal to the occlusion detects arterial wall motion as the cuff is deflated and flow resumes. Two crystals are implanted into the same transducer. One emits a short burst of very high frequency sound and the second receives the reflected sound energy. The reflected pulse is analyzed for frequency shift, and arterial wall motion is determined. Usually a 2 to 10 MHz ultrasound source and receiver are used. Since penetration of ultrasound is inversely related to frequency, and resolution is directly proportional to frequency, in small infants the higher ultrasonic frequencies give higher resolution with adequate pentration. In children and adults the 2 MHz system works best.

The Arteriosonde ultrasound blood pressure system (Roche Medical Electronics Inc.) was introduced in the early 1970s as one of the first "automatic" blood pressure devices. It included an arm cuff, pulse sensor, and processing system. The pulse sensor contained several ultrasonic emitters and receiver elements. It had the disadvantage (like most ultrasonic systems) of requiring conductive jelly placement between the sensor and the artery.

Once again, the accuracy depends on several principles. Measured systolic values can be lower than intra-arterial because distal blood flow lags behind the initial opening of the artery under the cuff. Diastolic values are frequently inaccurate because of the vague endpoint. There have been numerous studies comparing intra-arterial and indirect Doppler blood pressure with good correlation noted.[11,14,18,22,25,29,47] This method has been frequently used in infants because of the difficulty of hearing Korotkoff sound in these patients.[11]

Gordon et al[22] compared blood pressure measurements in 32 premature infants and found an average Doppler systolic blood pressure of 76.6 mm Hg versus 76.3 mm Hg for intra-arterial. The average diastolic Doppler pressures of 66.8 mm Hg compared with an intra-arterial value of 61.6 mm Hg. The correlation coefficients for Doppler versus intra-aortic were 0.98 and 0.93 for systolic and diastolic, respectively. Poppers[40] reported a good correlation for direct arterial pressure and Doppler-determined systolic and diastolic pressures in 12 children even when Korotkoff sounds were inaudible. Poppers et al[41] also studied 15 adults using the Arteriosonde-1217 comparing both manual auscultatory and direct intra-arterial measurements and reported good correlation. Hochberg and Salomon[26] reported an excellent correlation between direct pressure and indirect ultrasound methods of blood pressure determination. In their study, the mean systolic difference between the automatic blood pressure system and intra-arterial measurement was 0.5 mm Hg. Mean diastolic difference was 7.6 mm Hg. There was close correlation between the automatic ultrasound blood pressure determinations and Korotkoff-obtained pressures, although both gave higher values than intra-arterial methods.

Electrical interference from operating room electrosurgical equipment limits the usefulness of ultrasonic blood pressure systems. Many of the newer systems have auto-sensing systems that interrupt the current determination when electrical interference is detected.

Photoplethysmography provides another method for peripheral pulse detection. An occlusive cuff is used, along with a device that transmits light through the tissue distal to the artery. The light transmission is measured by a light detector as the cuff is deflated. With the passage of blood under the cuff, a change in light transmission occurs and systolic pressure is noted. This system measures only systolic pressure.

In 1959 Robinson described a simple device that could be constructed utilizing photoplethysmography and displayed the output on a graphic recorder or oscilloscope.[45] Since then, light sources and detectors have become simpler and now even a pulse oximeter can serve as the peripheral pulse detector. A recent study showed good correlation for systolic blood pressure determined by pulse detection with a pulse oximeter and by Doppler.[57] Wallace reported less difficulty when the loss of pulse was determined during inflation of the cuff with return of pulse with cuff deflation, since loss of pulse is immediately detected by the pulse oximeter.

Recently, Ohmeda has introduced an automated noninvasive blood pressure system that uses oscillometry for routine blood pressure determinations and a finger pulse detector for "stat" systolic determinations by detecting return of flow in the finger. The pulse detector appears similar to the standard Ohmeda pulse oximeter probe and is placed on a digit on the same extremity as the occluding cuff. This system has the benefit of both methods, that is, reliable systolic, diastolic, and mean pressure determinations by oscillometry and quick "stat" systolic determinations by return of pulse. Clinical trials with this device have yet to be reported.

Pitfalls of Occlusive Systems

Although easy to use, automated intermittent noninvasive systems have the potential to cause complications. Skin avulsion, ulnar neuropathy, and venostasis have all been reported.[3,4,7,50,52] These are usually considered to be secondary to frequent and prolonged determinations and have prompted manufacturers to decrease the time needed for a blood pressure determination. One manufacturer has decided not to include a continuous or "stat" mode [per, Invivo Research Labs]. Because the continuous mode repetitively cycles and deflation times can take 20 to 40 seconds, the total occlusion time can be excessive. In addition there are several other disadvantages: (1) not all pressures can be determined, for example, diastolic and mean pressure cannot be determined by palpation; (2) the accuracy is dependent on user ability to hear, feel, or see; and (3) beat-to-beat blood pressure measurement is not possible with palpation, auscultation, or return to flow. Even when these methods are automated the accuracy of blood pressures obtained suffers from three other factors: (1) there is no uniform method to detect diastolic pressure; (2) the pressures measured may be inaccurate since the automated devices sample pressures over multiple heart beats; and (3) these devices only provide information at best every 20 to 30 seconds.

NONOCCLUSIVE METHODS

The numerous disadvantages of the occlusive methods of blood pressure analysis, plus several personal factors, led to the development by Wesseling of the original nonocclusive device that could continuously measure blood pressure under clinical conditions. The first personal factor was simply a dream that blood pressure could be measured noninvasively on a continuous beat-to-beat basis. The second was a need to study the effects of a baroreceptor reflex mechanism on the control of blood pressure on a short-term basis. The third was a need for a device that would provide a continuous signal for a beat-to-beat pulse contour cardiac output computer.[59] The fourth personal factor was the need to develop continuous noninvasive techniques that removed the need for user skill in interpreting pressure. These needs, as well as the clinical needs of the anesthesiologist to have a continuous noninvasive measure of blood pressure available, have been addressed by the development of the automatic finger arterial blood pressure device Finapres (BOC Healthcare). Another device known as the Cortronic APM 770 (Cortronic Corp.) claims to measure blood pressure continuously from an upper arm cuff. The Finapres uses the Penaz method for blood pressure measurement while the Cortronic APM 770 uses a mathematical model for blood pressure determination. Both methods will be described in the following sections.

Penaz Method

The basis for the development of a nonocclusive blood pressure measurement system lies in Marey's work in the 1870s and 1880s.[34] Marey demonstrated a method using counterpressure to determine blood pressure. The counterpressure was applied to a sealed system in which the hand and forearm were immersed in water. As pressure in the system was increased, Marey observed oscillations in the recorded pressure caused by arterial pulsations. When the oscillations were at a maximum, the arterial wall was relieved of tension, and the blood pressure was transmitted directly to the water-filled chamber and then to a crude recording device.

Marey's unloaded arterial wall principle was not considered as the basis for continuous noninvasive pressure measurement until 1968, when Penaz described a method in which finger arterial blood pressure was measured continuously.[37] The method of Penaz was extended and refined by Wesseling, who used technical advances involving miniaturization of equipment and microprocessors to develop a clinically useful device.

Penaz constructed a device that consisted of a rigid, segmented cuff containing a light plethysmograph; a valve to control pressure in the cuff; a manometer; and a servo system to maintain the plethysmographic output constant (Fig. 3). The cuff is placed around a finger and inflated to a pressure equal to the pressure in the artery. Compressing the artery to its unstretched size ensures that the venous compartment is collapsed. With the artery unloaded, a potentiometer is set, based on the amount of light measured by the light plethysmograph. As intra-arterial pressure increases, the amount of blood entering the artery increases. This causes the finger to enlarge, thereby lengthening the distance between the plethysmograph sensor and light source. Therefore, the plethysmograph measures less light, and the signal output from the plethysmograph decreases. A difference from the set

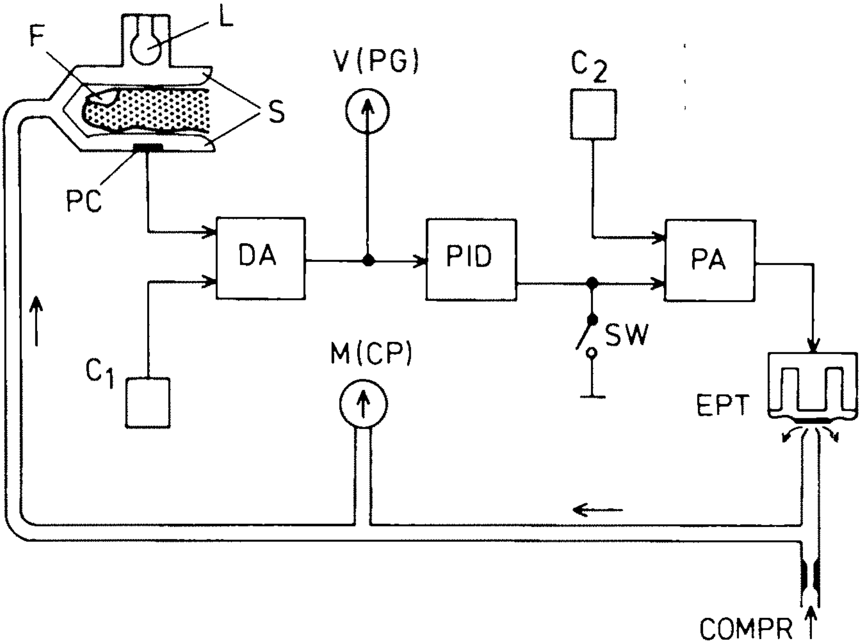


Figure 3. Original block diagram of the servo plethysmomanometer by Penaz. Following the arrows in the diagram a closed servo loop is traced. A finger (F) is shown in a rigid cuff (S) illuminated by a lamp (L). The plethysmogram is from a photocell (PC). In closed loop operation, with switch (SW) as shown, the output from the photocell is compared with a constant reference level (C_1). Any difference is amplified by a differential amplifier (DA) and shown on the volume output [V(PG)]. A electronic controller (PID), followed by power amplifier (PA), drives the electropneumatic transducer (EPT). Cuff pressure is read by manometer [M(CP)] supplied by a source of compressed air (COMPR).

point of the potentiometer now develops, the system is directed to increase the pressure in the cuff to maintain the zero gradient across the arterial wall. With fast processing, cuff pressure can follow intra-arterial pressure continuously.

The initial calibration of the potentiometer relies on the fact that zero transmural pressure across the arterial wall occurs somewhere between one half to one third of the unclamped or open volume of the artery. By observing the mean arterial pressure the Finapres measures the arterial volume changes from the plethysmograph and derives the open and collapsed arterial volumes. The device then sets the potentiometer at an appropriate value about halfway between these two volumes. During this state of zero transmural pressure, the pressure in the cuff is assumed to be identical to intra-arterial pressure, and thus calibrated blood pressure is measured noninvasively and continuously.

The Penaz method is simple in design but is difficult to implement, especially on a mass production basis. It required technical refinements of the cuff, valve, and servo mechanism. The cuff problems were overcome by the development of a multilayered plastic cuff that incorporates both the air bladder and the plethysmograph. The pneumatic valve was miniaturized to require a minimal amount of air to function. The servo system had to respond to pulse pressures over 200 mm Hg, and to arterial pressure waveform upstrokes with slopes up to 4000 mm Hg per second. A system bandwidth of 100 Hz was found to be necessary for the servo mechanism to maintain clinical accuracy. Finally, the entire system was automated using an Intel 8080-based 8-bit microcomputer.

Although the physiology of the Penaz method is not entirely understood, the device developed by Wesseling et al, and now commercially available under the trade name Finapres, operates as follows. A calibration or open mode searches for the cuff pressure that will result in a plethysmogram indicating near zero transmural pressure. This calibration mode is also known as the "lock procedure" and identifies that portion of the plethysmogram of maximum oscillations or mean arterial blood pressure.[33] Based on these initial measurements, the computer estimates the servo set point and closes the servo loop.

In the closed or servo mode the pressure in the cuff is automatically controlled so that the diameter of the artery remains near the set point pressure determined during the open mode. This is accomplished by maintaining the output from the photoplethysmograph constant and proportionally changing the pressure in the cuff in the same direction as the intra-arterial pressure. Initial clinical work with the prototype device indicated that there was a tendency for set point drift, particularly in the first 20 minutes of recording.[51] The open mode set point determination is now repeated at intervals to adjust for this drift as well as for other changes induced by cardiovascular stresses and reflexes.

Finapres Accuracy

The Finapres device has undergone numerous clinical trials comparing it with directly measured intra-arterial and conventional blood pressure measurements.[1,31,35,51,56,60] Initial studies in nonanesthetized patients used an early prototype device without the fast valve with a 25 Hz bandwidth. This study compared blood pressure measured from an indwelling brachial artery catheter to a prototype finger cuff positioned at heart level.[35] This study found that both systolic and diastolic finger blood pressures measured by the Penaz method underestimated invasively measured pressure by an average of 6 mm Hg. This statistically significant difference was thought to be due to the pressure gradient between the brachial artery and digital arteries. A subsequent study in anesthetized patients, with the hands lying by the patient's side, showed no difference in mean pressure between the Penaz method and intra-arterial pressure.[51] This difference between studies is related to the fact that the finger cuff acts like a pressure transducer. The brachial digital artery pressure gradient described previously was compensated for because the finger was lower than the heart.

Initial application of the Penaz method during anesthesia was performed by Smith et al[51] in 17 patients undergoing major surgery including open-heart procedures. Blood pressures obtained from two prototype Finapres devices were compared with pressures obtained from an indwelling radial artery cannula (Fig. 4). The prototype devices accurately and linearly tracked intra-arterial pressures over a wide range of pressures and during rapidly changing physiologic conditions. The offset error for mean pressure averaged 1 ± 4 mm Hg, with a standard deviation of 4 to 9 mm Hg. There was a mean correlation coefficient of 0.96, with a range of 0.89 to 0.98.

A subsequent study looked at 50 anesthetized patients, again

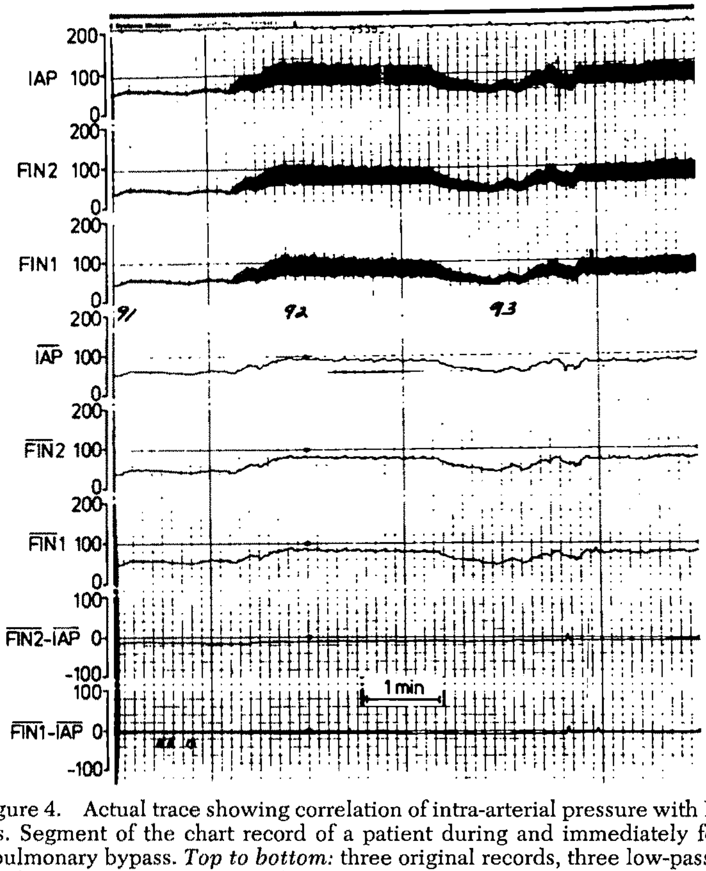


Figure 4. Actual trace showing correlation of intra-arterial pressure with Finapres devices. Segment of the chart record of a patient during and immediately following cardiopulmonary bypass. *Top to bottom:* three original records, three low-pass filtered records showing mean pressure, and two records from different channels. The full scale of all records is 200 mm Hg. Blood pressure samples (91, 92, and 93) were taken at the times indicated by the sample numbers handwritten below the third trace. The Finapres measured nonpulsatile pressures as accurately as pulsatile pressures. IAP = intra-arterial pressure. FIN1 and FIN2 = two Finapres prototypes. (*From* Smith NT, Wesseling KH, de Wit B: Evaluation of two prototype devices producing noninvasive, pulsatile, calibrated blood pressure measurement from a finger. J Clin Monit 1:17–29, 1985; with permission.)

comparing Finapres pressures with invasive radial artery pressures.[31] The thumb cuff was used because it has been suggested that the digital artery of the thumb will provide more accurate pressures, because it has a better supply from the radial artery.[49] In the study, cuffs were placed on the thumb as well as on other fingers on the same hand as the intra-arterial line. Overall, Finapres systolic and diastolic pressures differed from intra-arterial pressures by a mean of −4.8 mm Hg and 1.49 mm, respectively. However, the pressures obtained from the thumb cuff had the highest correlation coefficients for all pressures (systolic 0.95, diastolic 0.88, and mean 0.95) when compared with those obtained with cuffs placed on other fingers. The correlation coefficients for the latter ranged from systolic 0.50 to 0.92, diastolic 0.76 to 0.93, and mean 0.77 to 0.89.

Several studies have compared the Finapres with occlusive cuff methods. Arntzenius et al[2] found the systolic pressures obtained by the Finapres to be higher than the upper arm cuff measurements by an average of 6 mm Hg, while Finapres diastolic pressure was an average of 3 mm Hg less. Wesseling et al[60] also compared the Finapres with auscultatory blood pressure determinations in an ambulatory, elderly population. They concluded that finger systolic pressures were underestimated by a mean of 3 mm Hg and diastolic pressures were underestimated by an average of 5 mm Hg when compared with the auscultatory method. The authors suggested that the Finapres had several advantages over conventional blood pressure measurements.

There are other advantages related to the Finapres' ability to measure blood pressure continuously. Because the waveform was displayed, several patients with dysrhythmias were detected by the Finapres.[60] In addition, use of the Finapres eliminated the so-called cuff responders, that is, the individuals whose blood pressure increases when the blood pressure cuff is inflated. Johnson et al[30] showed that the Finapres was consistently able to reflect the transient changes in blood pressure and heart rate associated with epidural test doses of local anesthetics containing epinephrine.

Several investigators have examined factors that might affect the accuracy of the Finapres. These factors include prolonged measurement, effects of vasoactive drugs, the presence of a proximal arterial catheter, peripheral vascular disease, and rapidly changing clinical conditions. Finapres measurements have been evaluated over periods of up to 7 hours, with no reduction in accuracy noted.[51] Dorlas et al[10] studied the effects of infusion of phenylephrine on the accuracy of Finapres measurement compared with an automated upper arm blood pressure cuff. Following administration of the vasopressor, Finapres measurements of systolic blood pressure were on the average 7 mm Hg higher than the upper arm cuff and the mean diastolic pressures were 9 to 10 mm Hg below the upper arm cuff.

Kurki et al[31] compared the finger blood pressures with pressures obtained from a radial artery catheter after phenylephrine infusion and reported that there was a marked decrement in Finapres blood pressure. This was noted especially in patients with low intravascular volume. They suggested that the phenylephrine infusion caused peripheral vasospasm around the radial artery cannula and resulted in decreased peripheral blood flow. This situation should rarely occur, as one would not use both the Finapres and an intra-arterial cannula. In the same study, a temporary decrease in peripheral blood flow, as estimated by a Doppler velocity flow meter, was noted immediately following insertion of the intra-arterial cannula. This decrease was enough for the Finapres to alarm with a "no pulse" warning. Within several minutes the peripheral blood flow returned to a level sufficient to provide a signal for the Finapres to use. This phenomenon may be on the basis of vasospasm induced by the insertion of the cannula, with the vessel clamping around the cannula.

East et al[12] reported that in patients with peripheral vascular disease there was no statistically significant difference in pressure readings when the Finapres was compared with intra-arterial or oscillometric methods.

Three papers have reported on the accuracy of the Finapres during rapidly changing clinical conditions such as sudden hypotension, initiation of cardiopulmonary bypass, or initiation of one-lung ventilation during thoracotomy. Van Egmond et al[56] reported that the Finapres was able to closely reflect sudden changes in blood pressure. Smith et al[51] demonstrated that the Finapres was able to measure accurate blood pressure during and immediately following cardiopulmonary bypass, even when blood flow was nonpulsatile. The finger blood pressure device was also accurate in a case of extreme hypotension seen when a pulmonary embolus occurred. The authors concluded that proper performance of the Finapres was unaffected by anesthetic agents, hemodilution, shock, or wide swings of temperature and blood pressure during cardiac surgery.

Kurki et al[31] reported that the Finapres occasionally was not reliable during thoracotomy when one-lung ventilation was initiated and the PaO_2 suddenly decreased. This phenomenon did not occur consistently, and the mechanism is unknown. The Finapres values returned to normal after two-lung ventilation was re-established.

Because the finger cuff is continuously inflated at mean arterial pressure, the effects of prolonged application of the finger cuff have been studied. Long-term effects of continuous cuff inflation range from early clinical evidence of peripheral venous congestion to measured decreases in capillary blood PO_2.[24] The capillary PO_2 returned to normal within 30 seconds of the cuff's release. In awake subjects the Finapres has been used for up to 3 hours without reports of unpleasant sensations.[24] Although temporary reddening of the skin has been observed, there have been no reports of adverse sequelae following prolonged application of the finger cuffs.

In conclusion, the implementation of the Penaz-Wesseling unloaded artery method provides the clinician with an accurate, noninvasive, continuous beat-to-beat display of the arterial waveform and the systolic, diastolic, and mean blood pressures. It is accurate when compared with occlusive techniques or with intra-arterial pressures.

It does not use an occlusive cuff that would impede intravenous flow. In addition, the currently available device displays an arterial waveform that can be used for diagnostic purposes. The Finapres is a major step in noninvasive automated cardiovascular monitoring.

Cortronic

The Cortronic APM 770 is a recently patented device that claims to measure blood pressure on a continuous beat-to-beat basis by the use of an upper arm cuff. This is another device that essentially uses the oscillometric method described by Marey to determine systolic, diastolic, and mean blood pressures. The Cortronic uses the empirical parabolic equation:

$$y = Ax^2 + B$$

to model the displacement or oscillation, x, of an arterial wall as seen by a low pressure cuff, to the arterial pressure, y, causing the displacement. The coefficients A and B are dependent on arterial wall stiffness and smooth muscle tone of the individual patient. The prototype device used two cuffs, a normal sphygmomanometer upper arm cuff and a low-pressure cuff on the opposite arm. The systolic, diastolic, and mean blood pressures are determined by the oscillometric methods by gradually decreasing the pressure in the sphygmomanometer cuff. At the same time, the low-pressure cuff is inflated to approximately 20 mm Hg. As the blood pressures are being determined in the sphygmomanometer cuff, the characteristic of the waveform generated and the corresponding arterial wall displacement is noted by the low-pressure cuff, which then generates a computer "look-up" table. This look-up table consists of average displacements associated with average systolic and diastolic pressure from the peaks of the oscillations. The sphygmomanometer cuff is deflated, and only the low-pressure cuff remains inflated. The low-pressure cuff senses the arterial displacement, then by referring to the look-up table, blood pressures corresponding to that amount of arterial wall displacement measured earlier are determined. There are no data as to how this device responds to vascular changes, reflex or otherwise.

The currently available Cortronic device uses a single upper arm cuff to sequentially perform both high- and low-pressure measurements. Initial calibration is accomplished by inflating the high-pressure cuff above systolic arterial pressure. After cuff inflation, a 4 mm per second step-down of inflation pressure begins, and the waveform is sampled 64 times per second to generate the arterial wall characteristics. The low-pressure cuff is then inflated to 20 mm Hg and a servo mechanism maintains this pressure continuously. The device will automatically recalibrate at fixed intervals or at intervals selected by the user. It should be noted that during the calibration phase the patient must be stationary, since calibration is impossible with motion artifact. The manufacturer claims that the device provides continuous blood pressure determinations that correlate with intra-arterial values, although published data describing the Cortronic are limited. The manufacturer relates that it is not uncomfortable for long-term use. During orthopedic surgery involving frequent surgical manipulations it has been noted that the device can be inaccurate. This suggests that it is very artifact sensitive. The device also has difficulty measuring pressure in patients with large flabby upper arms or decreased muscle mass (personal communication, R. Carrcuci). Further work is needed before final judgment can be passed on this device.

REFERENCES

1. American Heart Association: Recommendations for human blood pressure determination by sphygmomanometers. Circulation 62:1146A, 1980
2. Arntzenius AC, Bonjer FH, Huige MC, et al: Measurement of blood pressure epidemiology of arterial blood pressure. Kesteloot H, van Joossens J (eds). The Hague, Martinus Nijhoff Publishers, 1980
3. Bause GS, Weintraub AC, Tanner GE: Skin avulsion during oscillometry. J Clin Monit 2:262, 1986
4. Betts EK: Hazards of automatic noninvasive blood pressure monitoring. Anesthesiology 55:717, 1981
5. Bruner JMR, Krenis LJ, Kunsman JM, et al: Comparison of direct and indirect methods of measuring arterial blood pressure, part III. Med Instrum 14:182, 1981
6. Burch GE, Shewey L: Sphygmomanometric cuff size and blood pressure recordings. JAMA 225:1215, 1973
7. Celoria G, Dawson JA, Teres D: Compartment syndrome in a patient monitored with an automated blood pressure cuff. J Clin Monit 3:139, 1987
8. Chungcharoen D: Genesis of Korotkoff sounds. Am J Physiol 207:190, 1964
9. Davis RF: Clinical comparison of automated auscultatory and oscillometric and catheter-transducer measurements of arterial pressure. J Clin Monit 1:114, 1985
10. Dorlas JC, Nijboer JA, Butijn WT, et al: Effects of peripheral vasoconstriction on the blood pressure in the finger, measured continuously by a new noninvasive method (the Finapres). Anesthesiology 62:342–345, 1985
11. Dweck HS, Reynolds DW, Cassady G: Indirect blood pressure measurement in newborns. Am J Dis Child 127:492, 1974
12. East TD, Pace N, Sorenson B, et al: Effect of peripheral vascular disease on accuracy of noninvasive, continuous, blood pressure measurement from the finger (Finapres). Anesthesiology 67:A186, 1987
13. ECRI: Automatic sphygmomanometers. ECRI Health Devices Report 15:187, 1986
14. Elseed AM, Shinebourne EA, Joseph MC: Assessment of techniques for measurement of blood pressure in infants and children. Arch Dis Child 48:932, 1973
15. Finnie KJC, Watts DG, Armstrong PW: Biases in the measurement of arterial pressure. Crit Care Med 12:965, 1984
16. Friesen RH, Lichtor JL: Indirect measurement of blood pressure in neonates and infants utilizing an automated noninvasive oscillometric monitor. Anesth Analg 60:742, 1981
17. Geddes LA, Voelz M, Combs C, et al: Characterization of the oscillometric method for measuring indirect blood pressure. Ann Biomed Eng 10:271, 1982
18. George CF, Lewis PJ, Petrie A: Clinical experience with use of ultrasound sphygmomanometer. Br Heart J 37:804, 1975
19. Gloyna DF, Huber P, Abston P, et al: A comparison of blood pressure measurement techniques in the hypotensive patient. Anesth Analg 63:222, 1984
20. Goldhill DR: Bilateral simultaneous indirect systolic blood pressure measurements. Cardiovasc Res 20:774, 1986

21. Goldthorp SL, Cameron A, Asbury AJ: Dinamap arm and thigh arterial pressure measurement. Anaesthesia 41:1032, 1986
22. Gordon LS, Johnson PE, Penido JRF, et al: Systolic and diastolic blood pressure measurements by transcutaneous Doppler ultrasound in premature infants in critical care nurseries and at closed-heart surgery. Anesth Analg 53:914, 1974
23. Gourdeau M, Martin R, Lamarche Y, et al: Oscillometry and direct blood pressure: A comparative clinical study during deliberate hypotension. Can Anaesth Soc J 33:300, 1986
24. Gravenstein JS, Paulus DA, Feldman J, et al: Tissue hypoxia distal to a Penaz finger blood pressure cuff. J Clin Monit 1:120–125, 1985
25. Gundersen J, Ahlgren I: Evaluation of an automatic device for measurement of the indirect systolic and diastolic blood pressure, Arteriosonde 1217. Acta Anaesthesiol Scand 17:203, 1973
26. Hochberg HM, Salomon H: Accuracy of an automated ultrasound blood pressure monitor. Curr Ther Res 13:129, 1971
27. Hutton P, Prys-Roberts C: The oscillometer in theory and practice. Br J Anaesth 54:581, 1982
28. Hutton P, Dye J, Prys-Roberts C: An assessment of the Dinamap 845. Anaesthesia 39:261, 1984
29. Johnson CJH, Kerr JH: Automatic blood pressure monitors: A clinical evaluation of five models in adults. Anaesthesia 40:471, 1985
30. Johnson PW, Hom M, Mulroy MF: Adequacy of automated blood pressure cuffs with epinephrine test doses in beta blocked patients. Anesthesiology 67:A187, 1987
31. Kurki T, Smith NT, Head N, et al: Noninvasive continuous blood pressure measurement from the finger: Optimal measurement conditions and factors affecting reliability. J Clin Monit 3:6–13, 1987
32. Loubser PG: Comparison of intra-arterial and automated oscillometric blood pressure measurement methods in postoperative hypertensive patients. Med Instrum 20:255, 1986
33. Mauck GW, Smith CR, Geddes LA, et al: The meaning of the point of maximum oscillations in cuff pressure in the indirect measurement of blood pressure—part II. J Biomech Eng 102:28, 1980
34. Marey EJ: La Methode Graphique. Paris, 1878
35. Molhoek GP, Wesseling KH, Settels JJ, et al: Evaluation of the Penaz servo-plethysmo-manometer for the continuous, non-invasive measurement of finger blood pressure. Basic Res Cardiol 79:598–609, 1984
36. Nystrom E, Reid KH, Bennett R, et al: A comparison of two automated indirect arterial blood pressure meters: With recordings from a radial arterial catheter in anesthetized surgical patients. Anesthesiology 62:526, 1985
37. Penaz J: Czech patent #133295. Prague, 1968
38. Perlman LV, Chiang BN, Keller J, et al: Accuracy of sphygmomanometers in hospital practice. Arch Intern Med 125:1000, 1970
39. Pederson RW, Vogt FB: Korotkoff vibrations in hypotension. Med Instrum 7:251, 1973
40. Poppers PJ: Controlled evaluation of ultrasonic measurement of systolic and diastolic blood pressures in pediatric patients. Anesthesiology 38:187, 1973
41. Poppers PJ, Epstein RM, Donham RT: Automatic ultrasound monitoring of blood pressure during induced hypotension. Anesthesiology 35:431, 1971
42. Ramsey M: Noninvasive automatic determination of mean arterial pressure. Med Biol Eng Comput 17:11, 1979
43. Ress J: Automated blood pressure measurements can be more accurate than manual measurements. Med Elect, April, 148, 1987
44. Riopelle JM: Modification of Dinamap for mechanical sphygmomanometry. Anesthesiology 57:245, 1982
45. Robinson RE, Eastwood DW: Use of a photo-sphygmomanometer in indirect blood pressure measurements. Anesthesiology 20:704, 1959
46. Rutten AJ, Ilsley AH, Skowronski GA, et al: A comparative study of the measure-

ment of mean arterial blood pressure using automatic oscillometers, arterial cannulation and auscultation. Anaesth Intens Care 14:58, 1986

47. Sheppard LC, Johnson TS, Kirklin JW: Controlled study of brachial artery blood pressure measured by a new indirect method. J Assoc Adv Med Instrum 5:297, 1971
48. Silas JH, Barker AT, Ramsay LE: Clinical evaluation of Dinamap 845 automated blood pressure recorder. Br Heart J 43:202, 1980
49. Shaw EF, Kaplan ED: The blood supply of the hand. *In* Kaplan ED (ed): Kaplan's Functional and Surgical Anatomy of the Hand, ed 3. Philadelphia, Lippincott, 1984, pp 203–221
50. Showman A, Belts EK: Hazard of automatic noninvasive blood pressure monitoring. Anesthesiology 55:717, 1981
51. Smith NT, Wesseling KH, de Wit B: Evaluation of two prototype devices producing noninvasive, pulsatile, calibrated blood pressure measurement from a finger. J Clin Monit 1:17–29, 1985
52. Sy WP: Ulnar nerve palsy possibly related to use of automatically cycled blood pressure cuff. Anesth Analg 60:687, 1981
53. Taguchi JT, Suwangool P: "Pipe-stem" brachial arteries—a cause of pseudohypotension. JAMA 228:733, 1974
54. Ur A, Gordon M: Origin of Korotkoff sounds. Am J Physiol 218:524, 1970
55. Van Bergen FH, Weatherhead DS, Treloar AE, et al: Comparison of indirect and direct methods of measuring of arterial blood pressure. Circulation 10:481, 1954
56. Van Egmond J, Hasenbos M, Crul JF: Invasive v. noninvasive measurement of arterial pressure. Comparison of two automatic methods and simultaneously measured direct intraarterial pressure. Br J Anaesth 57:434–444, 1985
57. Wallace CT, Baker JD, Alpert CC, et al: Comparison of blood pressure measurement of Doppler and by pulse oximetry techniques. Anesth Analg 66:1018, 1987
58. Wallace CT, Carpenter FA, Evins SC, et al: Acute pseudohypertensive crisis. Anesthesiology 43:588, 1975
59. Wesseling KH, de Wit B, Weber JAP, et al: A simple device for the continuous measurement of cardiac output. Adv Cardiovasc Phys 5:16–52, 1983
60. Wesseling KH, Settels JJ, Goedhard WJA: Nieuwe ontwikkelingen in het bloeddrunmeten in het bijsonder bij oudere mensen. *In* Goedhard WJA, Knook DL (eds): Bloeddruk en Hypertensie op Oudere Leeftijd. Stafleu, Alphen, 1984, pp 37–53
61. Yelderman M, Ream AK: Indirect measurement of mean blood pressure in the anesthetized patient. Anesthesiology 50:253, 1979

Department of Anesthesiology VA-125
3350 La Jolla Village Drive
San Diego, CA 92161

0889–8537/88 $0.00 + .20

Pulmonary Artery Catheter Monitoring

*Jeffery S. Vender, MD**

Quantitative assessment of hemodynamic function is essential for the successful management of high-risk surgical patients. Studies have shown that clinical observation is often subjective and frequently inadequate.[20,28,43] Medical therapy based on clinical assessment alone may be harmful.

Technological advances in cardiopulmonary monitoring have provided the anesthesiologist with the ability to rapidly assess multiple cardiorespiratory parameters. Cardiopulmonary monitoring may be noninvasive or invasive. Invasive monitoring should be reserved for situations in which noninvasive techniques cannot supply the needed information.

The development of flow-directed, balloon flotation pulmonary artery (PA) catheters has been a major advance in hemodynamic monitoring. Initially, the PA catheter provided the ability to assess intracardiac pressures. Many studies have demonstrated the advantages of PA catheters in assessing left ventricular preload and diagnosing hydrostatic pressure pulmonary edema. Right heart pressures are unreliable determinants of left ventricular filling pressures.[79] In patients with cardiopulmonary disease or in the elderly surgical patient, the central venous pressure (CVP) measurements may in fact vary inversely with the pulmonary capillary wedge pressure (PCWP).[18,31,71]

For the reasons cited, there has been a dramatic increase in PA catheter monitoring. In part, the clinical advantages of PA catheters include the ability to (1) measure intracardiac pressures, (2) determine cardiac output, and (3) obtain intracardiac and mixed venous blood samples. This information can be used to assess volume status and ventricular performance, calculate the derived hemodynamic and respiratory indices, and evaluate tissue oxygen balance. Optimal use of PA catheters depends on the following: (1) appropriate application of reliable data, (2) understanding what factors alter the validity of the measurements, and (3) understanding the complications associated

---

*Associate Professor, Clinical Anesthesia, Northwestern University Medical School, Chicago; Director, Intensive Care, Evanston Hospital, Evanston, Illinois

This article is modified from an article in *Critical Care Clinics,* 4:455–477, July 1988

with the use of PA catheters. Therapeutic decisions based on "numbers" alone are always inappropriate. PA monitoring must provide more than data points. In critically ill patients, it is essential to incorporate the data points with sound clinical judgment.

Since their introduction two decades ago, there has been a vast expansion in the clinical application of PA monitoring. Indications for PA monitoring are broadly defined in the current medical textbooks. PA monitoring can help define the etiology of the clinical problem, monitor the pathophysiologic progression, and guide in therapy as well as monitor the response to therapy.

This article focuses on (1) the validity and interpretation of data obtained from PA pressure monitoring, (2) physical complications of PA monitoring, (3) thermodilution cardiac output, (4) mixed venous oxygen saturation monitoring, and (5) clinical application of PA catheters.

DATA MEASUREMENT AND INTERPRETATION

The monitoring of intracardiac pressures, especially PCWP, is a primary function of PA monitoring. The accuracy and validity of the data are dependent on (1) the proper functioning of the pressure monitoring equipment, (2) an understanding of the various factors that alter the relationship between the PCWP and other cardiac pressures and volumes, and (3) obtaining the true PCWP from the tracing.

Technical errors due to pressure monitoring equipment occur quite commonly. Measurement errors can invalidate the clinical usefulness of data. The equipment necessary for PA catheter monitoring includes the catheter, the pressure transducer, tubing, flush system, connectors, and oscilloscope. A detailed discussion of the dynamic response characteristics (that is, natural resonant frequency, damping coefficient) of pressure monitoring systems is beyond the scope of this article and is reviewed elsewhere[34,54] (see the article by Horrow and Seitman in this issue).

"Catheter fling" and "dampened" tracings refer to alterations in the quality of the transduced pressure tracing. Damping can result from either air bubbles or a blood clot in the tubing system; loose, damaged fittings; long, narrow, compliant, or kinked tubing; excessive stopcocks; apposition of the catheter tip against the vessel wall; or inadequate flushing following aspiration of PA blood. Fling is produced by catheter motion during cardiac contraction. Systolic pressure values may be affected by both catheter fling and damping. Adequacy of dynamic response can be checked by assessing the system response following a rapid flush.[34]

Assuming a reasonable dynamic response of the catheter, accuracy is dependent on calibration of the transducer system. Static calibration usually requires two reference points: the zero point and the calibration point. The zero point is referenced to atmospheric pressure and the calibration point is determined by the pressure of a column of mercury applied to the transducer. Modern transducer amplifiers use internal electrical signals to simulate the calibration point. The transducer is zeroed at the midleft atrial level for central hemodynamic pressure monitoring. In the supine position, the midchest level, and the upright position, the midchest level at the junction of the sternum with the fourth intercostal space is used to determine the midleft atrial reference level.

HEMODYNAMIC PRESSURE MONITORING

The hemodynamic monitoring of high-risk patients assumes an appreciation of the various physiologic determinants of cardiac output, arterial pressure, and oxygen delivery (Fig. 1). Preload is defined as the initial ventricular fiber length at end-diastole and its direct effects on cardiac performance (Frank-Starling). Clinically, preload is determined by ventricular end-diastolic volume (EDV). EDV is difficult to measure routinely at the bedside. Changes in left ventricular EDV (LVEDV) will alter left ventricular end-diastolic pressure (LVEDP). The relationship of LVEDV to LVEDP is dependent on ventricular compliance (discussed later). PA catheter monitoring is used to measure PCWP as a reflection of LVEDP.

Figure 2 depicts the relationship between pulmonary artery end-diastolic pressure (PAEDP), PCWP, pulmonary venous pressure (PVP), and left atrial pressure (LAP) to assess ventricular preload. In the past, estimates of each of these pressures have been used as a guide to the LVEDP. The accuracy of these estimates is directly related to their proximity to the left ventricle.

Certain factors alter the ability to obtain accurate and meaningful

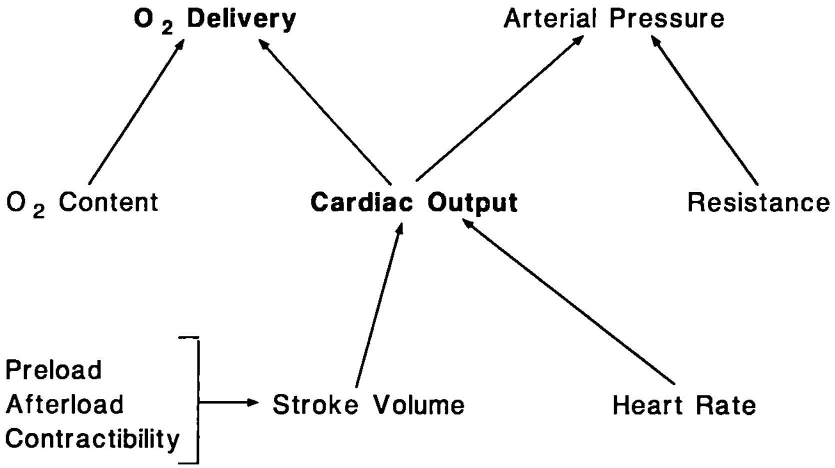


Figure 1. The primary determinants of cardiac output and oxygen delivery.

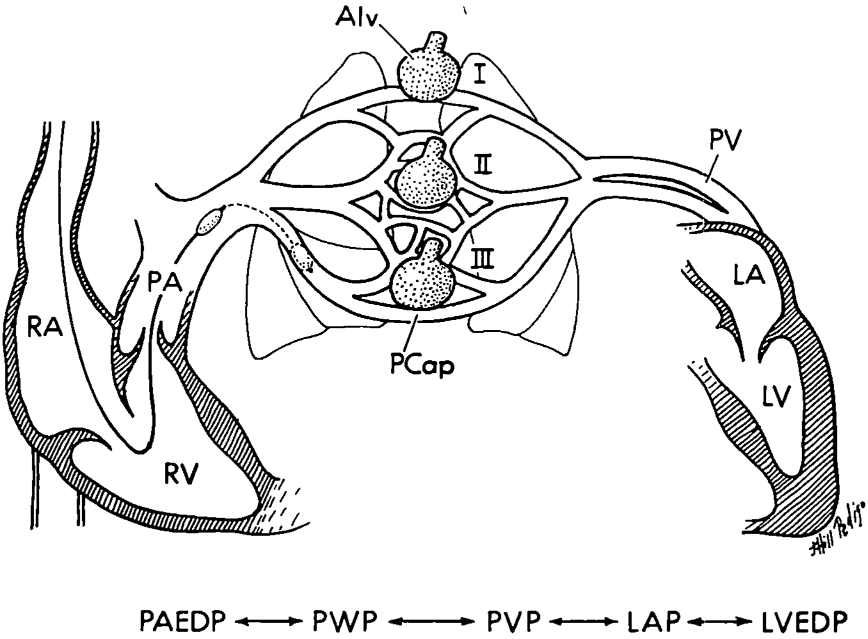


Figure 2. The anatomic position of a PA catheter in the pulmonary artery is demonstrated. The dotted line positions the inflated balloon in the "wedged" position. RA = right atrium, RV = right ventricle, PA = pulmonary artery, Alv = alveolus, PCap = pulmonary capillary, PV = pulmonary vein, LA = left atrium, LV = left ventricle, I, II, III characterize the relationship of $P_{alveolar}$, $P_{arterial}$, P_{venous} as described by West. The bottom is a progressive correlation of vascular pressures.

data from PA catheters. The following discusses these technical, physiologic, and pathologic factors.

As shown in Figure 2, the PA catheter in the proximal pulmonary artery bypasses the right heart chambers and valves. When the PA catheter balloon is inflated (PCWP) at end-diastole, there is cessation of forward blood flow in the "wedged" PA segment and a static fluid column exists between the left ventricle and the PA catheter tip. If there is no pressure gradient, then the PCWP will equilibrate with distal pressures (LVEDP). In healthy individuals, changes in the LVEDP are reflected by all proximal end-diastolic pressures (that is, PAEDP, PCWP, PVP, LAP, LVEDP). However, as with any static fluid column, alterations in the internal and external forces applied will diminish the ability of the catheter to reflect true LVEDP.

Under normal conditions, PAEDP is dependent on all distal pressures (for example, PVP, LAP, LVEDP). Normal pulmonary capillary resistance is minimal and impedance to flow limited.[30] Acute or chronic parenchymal pulmonary disease, pulmonary emboli, alveolar hypoxia, acidosis, hypoxemia, and vasoactive drugs can increase pulmonary vascular resistance (PVR).[60] An elevated PVR alters the direct relationship of PAEDP to PCWP. When heart rate is above 120, diastolic time is shortened, reducing the period for distal runoff. This also alters the relationship between PAEDP and PCWP. When PVR is increased, or when a significant tachycardia exists, the PAEDP cannot be assumed to reflect either the measured PCWP or any distal end-diastolic pressure.

The value of PCWP monitoring depends on accurate measurements and proper interpretation. The various factors that influence PCWP measurement and interpretation are well described.[9,15,48,57] Under normal circumstances, the PCWP reflects PVP and all distal pressures. The correlation between PCWP and PVP can be altered by PA catheter tip location, increased airway pressure (PEEP), and hypovolemia. West et al[85] described a gravity-dependent difference between ventilation and perfusion in the lung. Based on the relationship between pulmonary arterial (Pa), alveolar (P_{ALV}), and venous (Pv) pressures, West et al categorized these differences into three zones.[48] As depicted in Figure 2 in zone I alveolar pressure (P_{ALV}) exceeds Pa and Pv. In zone II P_{ALV} is greater than Pv but less than Pa. Only in zone III are Pa and Pv greater than P_{ALV}. In zone III, blood flow is uninterrupted, allowing the PA catheter tip to continuously communicate with distal vascular pressure. Pressures recorded in zones I and II can reflect alveolar more than vascular pressure. With increasing alveolar pressure (for example, PEEP) or decreased intravascular volume, zone III areas can revert to zone II or I. PA catheter tip position in zone III is essential for reliable PCWP monitoring. Because the catheters are flow directed, they tend to advance to areas of higher or continuous blood flow, which usually occur in a dependent area of the lung (zone III).

The following characteristics suggest a catheter tip outside zone III: (1) a smooth appearing PCWP tracing, (2) a PAEDP less than the PCWP, (3) an increase in PCWP greater than 50 per cent of the change in alveolar pressure, and (4) a decrease in PCWP greater than 50 per cent of the reduction in PEEP are all suggestive of a zone I or II catheter tip.[48] A lateral chest roentgenogram can help confirm the catheter tip location relative to the left atrium.[10] Increasing intravascular volume or decreasing alveolar pressure can convert zones I or II to zone III. Alternatively, the catheter or patient can be repositioned to place the catheter tip in a dependent position (zone III). Pulmonary catheter tip position may be less important in the patient with pulmonary parenchymal injury.[37] Many critically ill patients have noncompliant lungs, reducing the transmission of alveolar pressure to the pulmonary vasculature.[12] Finally, spontaneous ventilation or intermittent mandatory ventilation improves venous return and promotes normal pulmonary venous pressure.[9]

It is uncommon for a pressure gradient to develop between the pulmonary veins (PVP) and left atrium. However, occlusion of the pulmonary vein (for example, tumors, fibrosis, vasculitis, atrial myxoma) can cause PVP to exceed LAP.[57] Furthermore, it has been speculated that pulmonary venoconstriction occurs with endotoxemia and sepsis.[49]

Normally mean LAP approximates LVEDP. Valvular heart disease and alterations in ventricular compliance can alter the relationship between LAP and LVEDP. With mitral stenosis, LAP will exceed LVEDP. In patients with mitral insufficiency, ventricular systole causes retrograde ejection and alteration in diastolic filling and a LAP that can exceed LVEDP. This is detected by the presence of a large V wave on the PCWP tracing. A large V wave can mimic the PA tracing, leading to an erroneous interpretation. Aortic regurgitation and premature closure of the mitral valve cause a reverse pressure gradient (LVEDP greater than LAP) due to continued retrograde ventricular filling from the aorta.[30]

A decrease in left ventricular compliance can cause a disparity between LAP and LVEDP. Atrial contraction at end-diastole causes a greater increase in LVEDP (than LAP), augmenting ventricular filling and function. The "a" wave of the PCWP tracing best reflects the LVEDP in conditions associated with a decreased ventricular compliance, in the absence of pulmonary vascular obstruction or valvular heart disease.[27,57,62]

Accuracy of measured pulmonary pressure does not ensure that a linear relationship to ventricular volume exists. As defined earlier, preload is the length of the myocardial fiber at end-diastole. The fiber length is determined by the LVEDV. Therefore, the relationship between LVEDP and LVEDV is dependent on ventricular compliance (Fig. 3).

Under conditions of unchanging compliance, there is a curvilinear relationship between LVEDP (PCWP) and LVEDV. With increasing compliance, LVEDV can increase with minimal change in LVEDP (PCWP). The reverse occurs with decreased compliance: LVEDP (PCWP) increases with minimal change in LVEDV. A decrease in ventricular compliance always results in an increase in LVEDP. This explains the development of hydrostatic left ventricular pulmonary edema in patients with normal LVEDV. The nonlinear

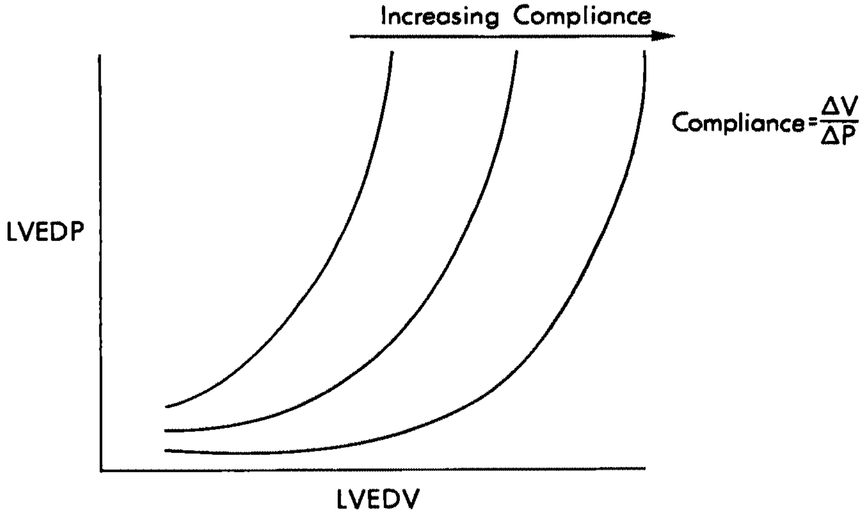


Figure 3. Typical series of left ventricular compliance curves.

nature of the compliance curve mandates that compliance cannot be thought of as a single number. Ventricular compliance is dynamic and changes abruptly with physiologic or therapeutic alterations.

Many factors have been identified that decrease ventricular complaince[9,15,42] (Table 1). Increased ventricular compliance is associated with the use of vasodilators (for example, nitroglycerin, nitroprusside), congestive myopathies, left-to-right interventricular septal shift, and regurgitant mitral or aortic valves.

LVEDP (PCWP) is an intravascular pressure. Transmural pressure is defined as the net distending pressure of the left ventricle. Transmural pressure is a true estimation of LVEDP, without the effect of pressure extrinsic to the heart. Transmural pressure results from subtracting the juxtacardiac pressure from intracavitary (LVEDP) pressure. Juxtacardiac pressure, the pressure surrounding the heart, is approximated by measuring the intrathoracic (intrapleural) pressure. During spontaneous ventilation the pleural pressure approaches zero at end-expiration. When this occurs, transmural pressure approximates LVEDP.[15,57]

The effects of PEEP on transmural ventricular pressure can affect the relationship of LVEDP (PCWP) to LVEDV. In addition to PEEP's effects on non-zone III lung, PEEP can alter ventricular distensibility by increasing juxtacardiac pressure and decreasing venous return. This causes a decrease in transmural pressure and a disproportionate increase in LVEDP (PCWP) relative to LVEDV (decreased compliance). The effects of PEEP on transmural pressure can be assessed by measuring pleural pressure. In clinical practice, pleural pressure is reflected by the midesophageal pressure obtained in the lateral decubitus position.[50] During PEEP therapy, the increase in LVEDP (PCWP) and effects on transmural pressure are limited by the pulmonary compliance and a reduction in venous return. As the lung becomes noncompliant, the effect of pleural pressure is reduced, and the PCWP (LVEDP) correlates better with transmural pressure. "Auto-PEEP" is a phenomenon in which mechanically ventilated patients progressively increase their intrathoracic pressure.[59] The mechanism is presumed to be due to air flow obstruction during expiration and residual air trapping. The effects of auto-PEEP on transmural and intrapleural pressure are similar to those described for PEEP. Clinically, PEEP levels less than 10 cm H_2O have a limited effect on intrapleural pressure, making LVEDP (PCWP) a close reflection of transmural pressure.

Alterations in ventilatory patterns can cause fluctuations in intrapleural pressure. Large swings in intrapleural pressure occur with

Table 1. *Decreased Left Ventricular Compliance*

Myocardial ischemia	Cardiac tamponade, effusion
Restrictive cardiomyopathy	Myocardial fibrosis
Right-left interventricular septal shift	Inotropic drugs
Aortic stenosis	Hypertension

positive pressure ventilation, labored respiratory efforts, Valsalva maneuver, and coughing. These fluctuations cause either an over- or underestimation of LVEDP (PCWP).

The best representation of transmural pressure requires the following steps. Whenever possible, measurements should be derived from a strip chart recorder or oscilloscope. Digital displays are inaccurate because they are time-based electrical samplings averaged over a predetermined interval. Measurements should be done at end-expiration. End-expiration will minimize the influence of intrapleural pressure swings and is usually identifiable on the oscilloscope. With spontaneous ventilation, the systolic peak is the best digital estimate of end-expiratory PCWP. During mechanical ventilation, the diastolic pressure is most representative of end-expiration. With quiet breathing or labored inhalation and expiration, it is often preferable to measure the mean PCWP. The most accurate determinations of transmural pressure are obtained from simultaneous recording of esophageal pressure (intrapleural pressure). Esophageal pressure is electronically subtracted from the PCWP, and the actual transmural pressure is determined (Fig. 4).

The effects of PEEP on PCWP can also be determined by measuring intrapleural pressure. Alternatively, adjusting the PCWP value based on the pulmonary compliance has been described.[16,42,57] With compliant lungs, half the PEEP is subtracted from the PCWP; with noncompliant lungs, a quarter of the PEEP is subtracted. Several investigations have recommended discontinuation of mechanical ventilation and PEEP during measurements of PCWP.[48] This is not recommended by this author. Acute changes in venous return can cause

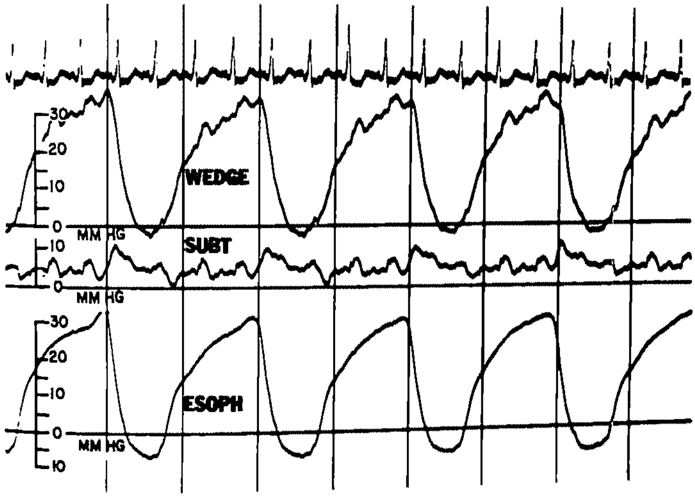


Figure 4. Simultaneous tracing of the measured PCWP and esophageal pressure. Electrical subtraction demonstrates actual transmural pressure with airway obstruction. (*From* Rice DL, Awe RJ, Gaaseld WH, et al: Wedge pressure measurement in obstructive pulmonary disease. Chest 66:628–632, 1974; with permission.)

an "autotransfusion effect" and potential cardiopulmonary decompensation. Abrupt discontinuation of high PEEP can alter respiratory mechanics and gas exchange.[22,57] More importantly, since the LVEDP (PCWP):LVEDV relationship is nonlinear and dependent on the state of ventricular compliance, it is more important to assess changes and trends in the PCWP relative to medical therapy (for example, volume, inotropes, vasodilators, diuresis, airway pressure change) and not be as concerned with the absolute number.

PHYSICAL COMPLICATIONS OF PULMONARY ARTERY MONITORING

The utilization of PA catheters is associated with numerous physical complications.[61,74] These complications are attributed to central venous cannulation (insertion), catheter passage (advancement), or catheter presence (maintenance). Numerous case reports have delineated a majority of the complications attributed to the use of PA catheters. Unfortunately, most published series review only a limited number of actual procedures. The frequency with which any particular complication occurs varies among the case reports and review articles in the literature. These complications are often classified as minor or major, depending on their potential for increasing morbidity or mortality. A recent prospective study reviewing 6245 PA catheter insertions reported a relatively low incidence of morbidity associated with PA catheters.[74] The simplicity and safety of PA catheter insertion have created a cavalier attitude among many professionals. The authors concluded that experience, supervision of trainees, and attention to detail were of primary importance in minimizing the incidence of complications.

Most complications can be avoided if physicians are cognizant of the risks, have an understanding of their mechanisms, and use techniques that reduce their occurrence. Every PA catheter insertion has the potential for a physical complication. Therefore, the benefits of PA monitoring need to be weighed against the risks. The following will briefly discuss physical complications of PA catheters.

Central Venous Cannulation

Complications of venous cannulation are identical for central venous access and PA catheter monitoring (Table 2). Amin et al[1] have delineated the advantages and disadvantages of the various venous access routes.

Table 2. *Complications of Central Venous Cannulation (Insertion)*

Arterial puncture
Pneumo-, hemothorax
Nerve injury
Air embolization
Horner syndrome
Mediastinal/pleural effusion
Chylothorax
Catheter embolization

Arterial puncture is a common complication of venous cannulation. With internal jugular vein cannulation, it is possible to enter the carotid artery. Likewise, subclavian vein cannulation can be associated with subclavian artery puncture. Arterial puncture is rarely a serious complication when small bore catheters are employed. Positional venous engorgement and small gauge "seeker" needles (22 g) minimize the incidence of unintentional or significant arterial punctures. The following techniques have been recommended to assure venous cannulation prior to insertion of a large bore (8.5 F) introducer: (1) transducing the pressure, (2) comparing the color of a blood sample with that of arterial blood, or (3) measuring comparative blood gas samples.[14]

Hemorrhage, hematoma formation with airway compromise, and embolization of atherosclerotic plaques are rare but occasionally reported sequela of unintentional arterial puncture. The presence of persistent subclavian artery bleeding and an occult hemothorax are clinically less obvious, more difficult to treat, and often are diagnosed by a subsequent chest roentgenogram. Coagulopathies can magnify the effects of arterial bleeding. Correction of a coagulation defect prior to cannulation can decrease the potential of hemorrhagic sequelae. When arterial punctures occur, local pressure is recommended. Local pressure is more effective with carotid artery bleeding, making internal jugular cannulation a safer procedure than subclavian vein cannulation. For surgical procedures requiring systemic heparinization (for example, cardiopulmonary bypass, major vascular cases), large bore arterial puncture is a relative indication for postponing the surgery. When surgery cannot be delayed, the neck should be prepped into the surgical field because of the increased potential of hematoma formation.[55]

Pneumothorax is a rare but well-recognized complication of venous cannulation by either subclavian or internal jugular approaches. Pneumothorax is less common with cannulation of the internal jugular vein.[1,39] Because of the potential for a pneumothorax (and the grave significance of a tension pneumothorax), a chest roentgenogram should be obtained following venous cannulation or insertion of a pulmonary artery catheter. If pneumothorax develops, a chest tube may be indicated, especially if the patient is receiving positive pressure ventilation or about to undergo general anesthesia.

Injury to other structures adjacent to the intended vascular route has been described. Trauma to the thoracic duct (left internal jugular approach) and subsequent chylothorax, Horner's syndrome, brachial plexus injury, and transient phrenic nerve injury are all recognized complications.[45,56] Misplacement of the catheter into the mediastinum or pleural space can result in the infusion of large volumes of fluid in nonvascular spaces (for example, hydrothorax, cardiac tamponade).[55]

Air embolization is a rare but potentially lethal complication.[25,35] Under certain conditions, CVP can become negative relative to atmospheric pressure, thereby creating a vacuum that can entrain air. The physiologic significance of air embolization is well described in the literature. Patients who have large negative pressure inspiratory efforts or who are dehydrated or in the sitting position are more prone to air embolization. Catheter placement in the Trendelenburg position or with the patient performing a Valsalva maneuver can limit the potential for air embolism. In addition to air, catheter shearing and embolization have been reported.[11] This complication is more common when catheters are withdrawn through metal introducer needles, but can occur with accidental misplacement of the retainer suture, or during a surgical procedure, near the insertion site. Finally, if the PA catheter balloon ruptures during insertion or with maintenance inflation, air can enter the circulation. This is rarely a problem, but in patients with right-to-left cardiac shunts it might be preferable to inflate the balloon with carbon dioxide.

Catheter Passage

Several of the complications noted with passage of the PA catheter can also occur with the catheter in place (Table 3). To avoid redundancy, these complications are discussed only once.

Arrhythmias are a frequent complication of PA catheter insertion and removal.[83] The reported incidence varies significantly, but appears to be influenced by the method of arrhythmia detection. Occasional premature contractions are often noted with balloon passage through the right ventricle, but reports of ventricular tachycardia are also common.[76] In addition, other arrhythmias (for example, premature atrial contraction, atrial fibrillation) and various conduction disturbances (right bundle branch block, complete heart block) have been reported.[55] Arrhythmias may be minimized by passing the catheter with the balloon inflated, rapid passage through the right ventricle, or withdrawal of the catheter and reinsertion after the administration of intravenous xylocaine. Studies have suggested that the routine use of prophylactic xylocaine prior to catheter insertion is ineffective.[70,74] If there is potential for complete heart block developing, a catheter with pacing capabilities can be used.

Coiling, looping, or knotting can occur during insertion of PA catheters. These complications are more common in low-flow states, patients with large intracardiac cavities, smaller PA catheters, or where an excessive length of catheter is inserted without obtaining the anticipated pressure tracing or position.[1,55] Although usually not necessary, fluoroscopy can be employed to determine catheter posi-

Table 3. *Complications of Catheter Passage (Advancement)*

Arrhythmias/heart block
Knotting/kinking
Valvular damage
Perforation of PA vessel

tion and guide direction during difficult insertions. A more significant sequela is the knotting of catheters around other structures (indwelling catheters, pacing wires, papillary muscles, chordae tendineae).[72] If the knot cannot be withdrawn directly through the original venotomy site, a fluoroscopic disentanglement or surgical removal may be needed. Aberrant PA catheter location during insertion such as pleural, pericardial, peritoneal, and inferior vena cava has been reported.[74] The proper placement of a PA catheter requires confirmation by a postinsertion chest roentgenogram.

Ventricular enlargement, low-output states, congenital cardiac defects, tricuspid insufficiency, and venospasm (peripheral veins) can increase the difficulty of passage. With difficult passage, patient repositioning (for example, head up, left side down), deep breathing, or fluoroscopic guidance may be necessary.

Catheter Presence in the Pulmonary Artery

The potential for morbidity and even mortality is present during the routine use of PA catheters (Table 4). A common but usually asymptomatic problem is venous thrombosis at the site of PA insertion.[17] Depending on the degree and location, the thrombi can alter transduced pressure tracings or the accuracy of thermodilution cardiac output. The incidence of this thrombogenesis is reportedly reduced by the use of heparin-bonded catheters.[40] Another form of thromboembolic pathology can result from distal migration of the PA catheter tip or prolonged balloon inflation occluding distal blood flow in the PA. Pulmonary infarctions can be a serious sequela, especially in low-flow states in which collateral blood flow is reduced. This complication can be limited by continuous monitoring of the PA trace, avoidance of prolonged balloon inflation, proximal catheter placement, and the use of continuous high-pressure heparin-flush devices.

Catheter-related infections, sepsis, and endocarditis are recognized causes of morbidity.[21] Colonization of the catheter is common. The following factors are reported to influence the incidence of catheter-induced infections: catheterization greater than 72 hours, multiple catheter manipulations, nonaseptic insertion and maintenance, system (infusion sets, cardiac output syringe) contamination, and skin puncture site infections. Surgical cutdowns have higher infection rates.[6] The suggested benefits of protective catheter sheaths are yet to be conclusively determined.[38] The factors for infection are significantly related to the incidence of endocarditis. Catheter-induced endocardial damage with subsequent septicemia appears to increase the

Table 4. *Complications of Catheter Presence in the PA (Maintenance)*

Thrombosis	Pulmonary infarction
Pulmonary artery rupture	Hematologic
Sepsis	Valve damage
Endocarditis	Thromboembolism
Balloon rupture (L-R shunt)	Arrhythmia

potential of endocarditis. With line changes, a new insertion site is preferable, although recent data suggest possible reuse of the old site with a guide wire change.[19]

The most dramatic and acutely catastrophic complication is pulmonary artery perforation and hemorrhage. Barash et al[7] have delineated several mechanisms for PA perforation during insertion or maintenance of PA catheters. Factors that increase the risk of PA perforation include advanced age, pulmonary hypertension, hypothermia, and deviations from standard insertion techniques. Patients who are anticoagulated or have coagulapathies may have a higher mortality rate.[28,68] Several suggestions to avoid this complication include patient selection; utilization of the PA diastolic pressure (where consistent with the pulmonary wedge pressure) to minimize the frequency of balloon inflations; continuous monitoring of the PA tracing; 1.5 ml balloon inflation to ensure proximal catheter tip location in the PA with initial placement; slow progressive balloon inflation during wedge recordings; and preinsertion determination of a concentric balloon. "Overwedging" is usually a sign of a distal catheter placement or balloon herniation over the tip causing a falsely elevated PA pressure (Fig. 5). This is caused by failure of the catheter tip to communicate with the arterial lumen. With balloon inflation, volume from the continuous-flush device is trapped between the balloon and vessel wall, causing a rapid, unstable increase in the PCWP. When overwedging occurs, the balloon is immediately deflated, withdrawn 1 to 2 cm, and reinflated slowly. Coagulation defects and volume loss should be corrected. On rare occasions a double-lumen endotracheal tube can be inserted to separate the bleeding from normal lung to preserve gas exchange. If massive bleeding develops, surgical intervention could be needed.[24] Supportive care is usually enough to manage most PA perforations.

Other less common complications are reviewed in the previously referenced articles. The actual incidence of serious or fatal complications is undefined, but the known potential necessitates constant attention to detail and patient selection based on a risk-benefit analysis.

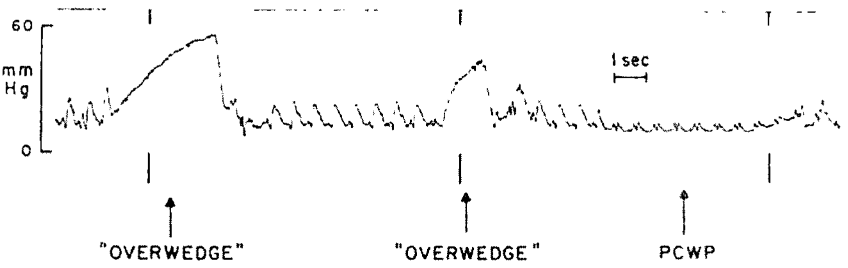


Figure 5. PA pressure tracing. With balloon inflation, the catheter "overwedges." The catheter is withdrawn and the normal PA and PCWP tracings are evident. (*From* Barash PG, Nardi D, Hammond G, et al: Catheter-induced pulmonary artery perforation, mechanisms, management and modifications. J Thorac Surg 82:5–12, 1981; with permission.)

PRINCIPLES OF THERMODILUTION CARDIAC OUTPUT

PA catheters have provided clinicians the ability to practically, rapidly, and accurately measure multiple cardiac outputs in the critical care environment. Thermodilution cardiac output has been shown to be an acceptable substitute to the less accessible use of the Fick principle or dye dilution.[33,77] Many of the derived hemodynamic indices and clinical therapies in critically ill patients are dependent on an accurate measurement of cardiac output.

The Stewart-Hamilton equation is the formula linking cardiac output to temperature. The equation is represented as the following:

$$Q = \frac{V\,(T_B - T_I)\,K_1\,K_2}{T_B\,(t)\,dt}$$

where Q = cardiac output, V = volume injected, T_B = blood temperature, T_I = injectate temperature, K_1, K_2 = computational constants, and $T_B(t)dt$ = change in blood temperature as a function of time. The thermodilution technique uses cold to create a thermal deficit as a variant of the indicator dilution technique. A cardiac output compute integrates the information to provide a cardiac output curve. The area under the curve is inversely proportional to the cardiac output.

Several technical considerations must be understood to minimize the potential for error with thermodilution cardiac output. The catheter thermistor must be positioned freely in the lumen of the PA. Falsely elevated cardiac outputs will occur if the thermistor impinges on the vessel wall, insulating it from the "cool" thermal indicator. Irregular cardiac output curves caused by poor injectate-blood mixing, thermistor-vessel wall contact, changes in heart rate or blood pressure, and abnormal respiratory patterns can produce inaccurate cardiac outputs.[65]

Injectate volume and temperature have been shown to affect thermodilution cardiac output measurements.[65] Typically, 10 ml of D5W is employed for thermodilution cardiac output. Smaller volumes (2.5 to 5 ml) can be used in situations in which volume overload is a concern without significantly affecting the results (for example, pediatrics). Careful filling of syringes is necessary to avoid error induced by variable injectate volumes. Injectate temperature can range from 0 to 24°C. The colder the injectate, the greater the signal-to-noise ratio and the better the accuracy and precision. Under most clinical conditions, 10 ml of room temperature injectate will provide an acceptable measurement. The following problems have been associated with cold injectates: (1) output error induced by injectate warming in the operators hand or catheter (after the computer has been programmed); (2) the time and cost needed to prepare and maintain the cold injectate; and (3) the potential for various arrhythmias. Supraventricular tachyarrhythmias and bradycardia post-cold injectate have been reported.[65] When patients are hypothermic (cardiopulmonary bypass), cold injectates may be necessary to increase the signal-to-noise ratio.

The actual speed of injection appears to be of minimal consequence if delivered in less than 4 seconds (10 ml).

Timing of injection to the respiratory cycle can improve the reproducibility of cardiac output measurements.[4] Because the temperature of PA blood can vary with phases of the respiratory cycle, it has been suggested that cardiac output measurement be timed at the same point in the respiratory cycle (for example, end-expiration). With positive pressure ventilation, a variation in thermodilution cardiac output has been correlated with cyclic variations in right ventricular cardiac output.[75] Because it is difficult to synchronize injection with end-expiration, particularly in a patient on mechanical ventilation, it has been suggested that the average of three evenly spaced determinations represents an accurate estimate of cardiac output. Modern computers help compensate for some of the respiratory-induced temperature shift by averaging the blood temperature for a short period of time prior to injection.[65]

The computational constant programs the cardiac output computer to the capacity of the injectate lumen as well as the injectate volume and temperature. Entering the wrong constant into the computer can produce inaccuracies in thermodilution cardiac output. Differences in the determination of various computation constants might explain the variations reported between different brands of computers.[51]

The percutaneous introducers commonly employed for the insertion of a PA catheter can precipitate errors in thermodilution output. Sideport extensions are frequently used for volume infusion. Depending on the rate and temperature of the infused volume, the measured thermodilution output will be altered. If the proximal port of the PA catheter is contained within the introducer sheath, the potential for retrograde injection into the side arm and sheath will produce an erroneously high output due to a measurement calculated on a smaller than anticipated volume (see Stewart-Hamilton equation). An irregular output curve demonstrating flattening and scalloping, a rising CVP measured via the side port during injection, and fluid in the side port are characteristic of this problem. This problem can be limited by withdrawal of the introducer sheath after PA catheter insertion or utilization of catheters with more distal injection ports.[78]

Certain conditions prevent appropriate mixing or directional flow of the indicator solution. Intracardiac shunts, tricuspid regurgitation, and cardiac arrhythmias, which affect beat-to-beat cardiac ejection, can all alter the accuracy of thermodilution cardiac output.

Cardiac output measurements are commonly used in clinical care. Cardiac output is determined by stroke volume and heart rate. Cardiac index (cardiac output/body surface area) attempts to equalize variations in body mass. Cardiac output is a primary determinant of oxygen delivery and is essential for the calculation of systemic vascular resistance (SVR), pulmonary vascular resistance (PVR), and stroke work index (SWI).

As a singular parameter, the clinical application of cardiac output has limitations. Cardiac output (index) can be a misleading indicator of myocardial function. A tachycardia can compensate for a stable or decreased stroke volume due to altered preload or contractility. The appropriate clinical utilization of cardiac output necessitates its combination with other measured (for example, $S\bar{v}O_2$, urine output) or derived indices to assess adequacy of tissue perfusion. A cardiac index of 4.0 L per minute per m^2 suggests excellent myocardial function, but could be luxuriant, adequate, or suboptimal depending on the tissue metabolic needs and arterial oxygen content (see $S\bar{v}O_2$ discussion).

Mixed Venous Oxygen Saturation ($S\bar{v}O_2$)

Routine measurement of cardiac filling pressures and cardiac output does not reflect adequacy of perfusion. Similar to minute ventilation, cardiac output provides a total measurement of flow. Multiple factors affect the determination of minute ventilation and cardiac output. Anesthesiologists rarely discuss minute ventilation but are more concerned with the $PaCO_2$ which is determined by adequacy of minute ventilation in relationship to metabolic rate. Interestingly, cardiac output is often the focal point in the diagnostic and therapeutic assessment of the high-risk surgical patient. As can be seen in Figure 6, cardiac output is positioned parallel to minute ventilation. Cardiac output is determined by stroke volume times heart rate. What is needed is a parameter comparable to $PaCO_2$ that will help determine adequacy of perfusion as a relationship to metabolic rate. In this regard, $S\bar{v}O_2$ has been offered as a parameter that can help assess the balance of the adequacy of tissue oxygen supply and demand dynamics.[43]

PA catheters provide access for the intermittent sampling of mixed venous blood from the PA. Progressive advances in fiberoptic technology have led to the development of catheters that continuously measure mixed venous oxygen saturation ($S\bar{v}O_2$).[73] Accuracy of these in vivo continuous oximeters versus bench oximeters has been documented.[5]

The ability of $S\bar{v}O_2$ to reflect total tissue oxygen balance necessitates an understanding of oxygen delivery, demand, and consumption.

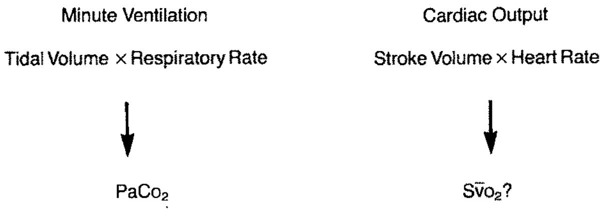


Figure 6. Similarities between minute ventilation and cardiac output (see text).

Oxygen delivery ($\dot{D}O_2$) equals the arterial oxygen content times cardiac output (CO):

$$\begin{aligned}\dot{D}O_2 &= (\text{Hgb} \times 13.8)\ \text{Sa}O_2 \times \text{CO} \\ &= (15 \times 13.8)\ (1) \times 5 \\ &= 1000\ \text{ml/minute} \end{aligned} \tag{1}$$

The 13.8 constant is a product of the 1.38 ml of O_2 per gram of hemoglobin (Hb) times a factor of 10 to convert the units for Hb to grams per liter. This equation does not include dissolved oxygen content, which is usually insignificant. Therefore, oxygen delivery is determined by CO, Hb, and the saturation of the Hb. The saturation of Hb is determined by the $\text{Pa}O_2$ and the oxyhemoglobin dissociation curve. The $\dot{D}O_2$ must be adequate to meet the amount of oxygen needed for cellular metabolism of the various organ systems (O_2 demand). Oxygen consumption ($\dot{V}O_2$) is the amount of oxygen actually utilized by the tissues for cellular metabolism. $\dot{V}O_2$ is determined by the amount of arterial $\dot{D}O_2$ to the tissues minus the venous $\dot{D}O_2$ to the heart:

$$\begin{aligned}\dot{V}O_2(\text{ml}/O_2) &= [(\text{Hb} \times 13.8)\ \text{Sa}O_2 \times \text{CO}] - [(\text{Hb} \times 13.8)\ \text{S}\bar{v}O_2 \times \text{CO}] \\ &= (\text{Hb} \times 13.8)\ \text{CO} \times (\text{Sa}O_2 - \text{S}\bar{v}O_2) \end{aligned} \tag{2}$$

Further derivation of equation 2 shows the relationship of $\text{Sv}O_2$ to the other indices:

$$\text{S}\bar{v}O_2 = \text{Sa}O_2 - \frac{\dot{V}O_2}{(\text{Hb} \times 13.8 \times \text{CO})} \tag{3}$$

$\text{S}\bar{v}O_2$ varies directly with cardiac output, hemoglobin, and $\text{Sa}O_2$ and inversely with metabolic rate. The normal $\text{S}\bar{v}O_2$ is 75 per cent ($\text{P}\bar{v}O_2 =$ 40 mm Hg), which indicates that normal metabolic needs are met by extraction of 25 per cent of delivered oxygen. An increase in oxygen demand or decrease in arterial oxygen content is compensated initially by an acute increase in cardiac output or oxygen extraction. In critically ill patients, cardiac reserves can be limited. If oxygen extraction increases, the $\text{S}\bar{v}O_2$ will fall. Reportedly, at a critical level of oxygen delivery, extraction of oxygen decreases, the $\text{S}\bar{v}O_2$ plateaus, and $\dot{V}O_2$ is delivery dependent.[53] When the $\text{S}\bar{v}O_2$ is 30 per cent or less, tissue oxygen balance is compromised and there is an increased potential for anaerobic metabolism and lactic acidosis.[52]

Figure 7 shows an $\text{S}\bar{v}O_2$ recording from a postcoronary artery bypass patient. Despite acceptable cardiac output determinations, this patient demonstrates a significant decrease in the baseline $\text{S}\bar{v}O_2$, which suggests an imbalance of tissue oxygen supply and demand. The metabolic rate has significantly increased with the onset of shivering. The inability to compensate for the increased oxygen demand by increasing cardiac output and the response to therapy are clearly tracked by the changes in $\text{S}\bar{v}O_2$. When $\text{S}\bar{v}O_2$ falls, one must consider all variables that alter oxygen supply or demand: cardiac output, hemoglobin, arterial saturation, and metabolic rate. When arterial O_2

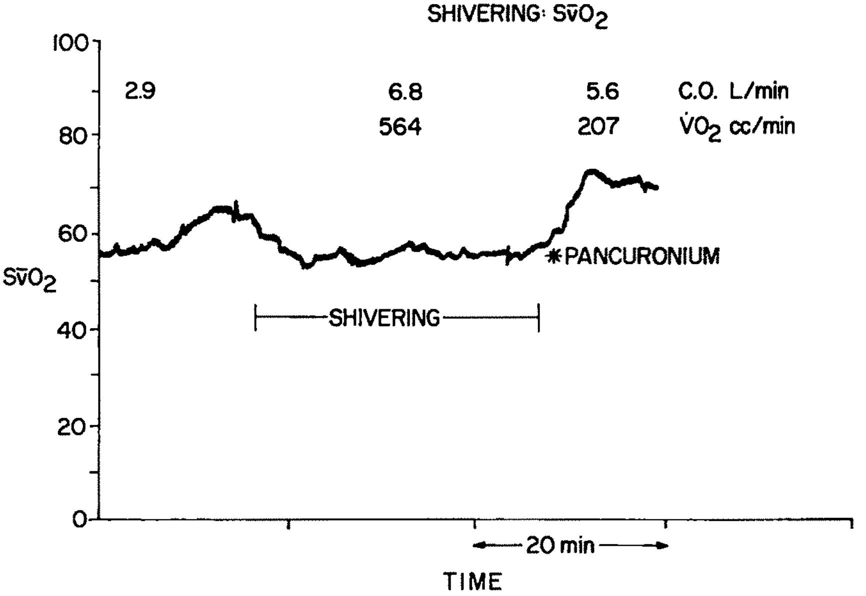


Figure 7. This $S\bar{v}O_2$ recording in a postcoronary artery bypass patient demonstrates the effects of shivering and its treatment, the relationship between $S\bar{v}O_2$, cardiac output (CO) and metabolic rate $\dot{V}O_2$.

content and $\dot{V}O_2$ are stable, $S\bar{v}O_2$ will correlate directly with fluctuations in cardiac output. As demonstrated, each of these variables will influence $S\bar{v}O_2$ changes.

Situations with increased $S\bar{v}O_2$ are more difficult to interpret. Sepsis, arterial-venous fistulae, cirrhosis, left-to-right cardiac shunts, peripheral shunts, cyanide poisoning, hypothermia, unintentional PA catheter wedging, and rapid withdrawal from the PA catheter of arterialized blood are a few situations that have been associated with an increased $S\bar{v}O_2$.[43] It is important to remember that $S\bar{v}O_2$ monitoring requires a true mixed venous sample to be valid.[26] Inadequate mixing of the SVC, IVC, and coronary sinus make measurements from the right atrium inaccurate. The presence of intracardiac shunts makes the determination of a "true" $S\bar{v}O_2$ from the PA impossible.

$S\bar{v}O_2$ can be used as a trend monitor or for diagnostic (for example, acute ventricular septal defect) and therapeutic assessments in critically ill patients.[13,73] Combining a pulse oximeter and $S\bar{v}O_2$ oximeter (dual oximetry) has provided a new monitor of the cardiopulmonary effects of PEEP in the management of acute respiratory failure.[64] $S\bar{v}O_2$ measured via PA catheters does not detect alterations of inadequate regional perfusion. It should be regarded as an index of adequacy of total tissue oxygen balance.

Clinical measurement of cellular (mitochondrial) oxygen is unavailable. Multiple indices have been suggested to reflect adequacy of tissue oxygenation (for example, $P\bar{v}O_2$, $S\bar{v}O_2$, oxygen extraction ratio, lactic acid, arterial-venous oxygen content). A discussion of which is the best index is beyond the scope of this article. At present, $S\bar{v}O_2$ is the only index clinically available on a continuous, real time basis.

Clinical Application of Pulmonary Artery Monitoring

The clinical utilization of PA catheter monitoring is well described in anesthesia, cardiovascular, and critical care journals and textbooks. Typically, PA catheter use is directed toward specific disease entities (for example, congestive heart failure, pulmonary edema, valvular dysfunction, adult respiratory distress syndrome, sepsis). Appropriate application should be predicated on the physiologic information obtained from the catheter for the diagnosis and management of the underlying pathology.[2,41] The following briefly discusses some of the common uses for PA catheters, and is not inclusive of all applications.

Volume assessment and fluid management are the most common applications of PA catheters. Support of tissue perfusion is the primary goal of fluid therapy discussed. As discussed previously, monitoring of PCWP as an indirect reflection of LVEDV has its limitations. At the extremes, therapy can be guided by the measurement of PCWP. More commonly, it is essential to follow the response of PCWP, cardiac output, and parameters of tissue perfusion to rapid fluid administration.

In conditions of inadequate tissue perfusion, the response of PCWP to a "fluid challenge" can be used to assess and guide therapy.[84] Fluid is administered in predetermined increments (50 to 200 ml) rapidly (10 minutes), and the change in PCWP is monitored. The magnitude of change in PCWP is determined by the patient's individual ventricular compliance curve. A large increase in PCWP (response greater than 7 mm Hg) or the development of pulmonary edema suggests an excessive LVEDP (preload) and a position on the steep portion of the ventricular function curve (Fig. 3). Further volume administration will increase LVEDP, heighten the risk of hydrostatic pulmonary edema, and increase myocardial oxygen consumption without any further improvement in cardiac output. Moderate increases in PCWP are of limited risk if they return within 10 minutes to within 3 mm Hg of the original value. If the PCWP does not increase at least 3 mm Hg and perfusion remains inadequate, additional "challenges" are necessary until return of systemic perfusion.

Once volume optimization has occurred and tissue perfusion remains inadequate, further therapeutic interventions are required. Augmentation of stroke volume may be accomplished by inotropic support, afterload reduction, and chronotropic modification. Measurement of cardiac output and calculation of systemic vascular resistance and stroke work index can help assess the effectiveness of these therapies.

PA catheters can be used for the early diagnosis and monitoring for myocardial ischemia.[44] An acute increase in PCWP or alterations in the PCWP tracing can precede the onset of electrocardiographic change suggestive of myocardial ischemia. Ischemia produces an acute decrease in ventricular compliance. LVEDP (PCWP) rises disproportionately to LVEDV. Additionally, an acute alteration in ventricular compliance can produce "a" waves on the PCWP tracing. Papillary muscle dysfunction due to subendocardial ischemia can produce mitral insufficiency and prominent large V waves. The presence of normal ventricular function in patients with significant coronary artery disease does not obviate the use of PA catheters for the monitoring of myocardial ischemia.[47] Although changes in ventricular compliance and wall motion abnormalities are reportedly more reliably detected with echocardiography, this modality is currently not available for routine, broad-based clinical application.

The measurement of intracardiac pressure can help distinguish cardiogenic from noncardiogenic pulmonary edema. Lung water is directly related to PCWP.[27] This relationship is magnified in conditions of leaky alveolar-capillary membranes. With acute lung injury (adult respiratory distress syndrome) pulmonary edema occurs with normal PCWP. Cardiogenic pulmonary edema is associated with an elevated PCWP. The optimal ventricular filling pressure is produced by an LVEDV adequate for tissue perfusion (cardiac output), which does not result in hydrostatic pulmonary edema.

Other diagnostic uses of PA catheters include (1) differentiation of a ventricular septal defect from mitral insufficiency and (2) the presence of cardiac tamponade. A new systolic murmur following a myocardial infarction can be due to a ventricular septal defect or acquired mitral insufficiency. With a ventricular septal defect, blood drawn from the various cardiac chambers shows a "step-up" in oxygen saturation between the right atrium and pulmonary artery, due to left-to-right shunting of highly oxygenated left ventricular blood across the ventricular septum. The magnitude of the shunt can be estimated from:

$$\text{SHUNT} = \dot{Q}_p/\dot{Q}_s = \frac{\text{Sa}O_2 - S_{RA}\,O_2}{\text{Sa}O_2 - S\bar{v}O_2}$$

where $\dot{Q}_p/\dot{Q}_s$ = ratio pulmonary to systemic blood flow, $\text{Sa}O_2$ = arterial O_2 saturation, $S\bar{v}O_2$ = mixed venous O_2 saturation, and $S_{RA}\,O_2$ = right atrial O_2 saturation.

If the murmur is due to acute mitral insufficiency, there is no step-up in O_2 saturation and a large V wave can be noted on the PCWP tracing (Fig. 8). Cardiac tamponade is definitively diagnosed by echocardiography. The equalization of all diastolic pressures (right atrium, right ventricle, PAEDP, PCWP) is highly suggestive of a constrictive cardiac process.

PA catheter monitoring has been used for the classification of hemodynamic function after myocardial infarction.[32] Clinical subsets correlating PCWP and cardiac index can aid in therapy selection and determining prognosis. Del Guercio et al[23] have demonstrated the

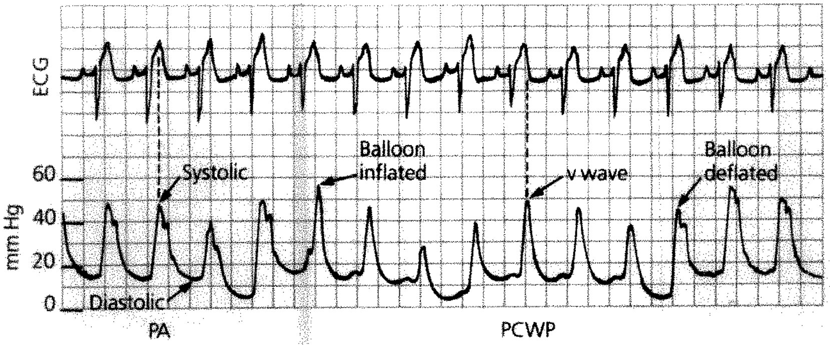


Figure 8. PA and PCWP tracings in a patient with acute mitral regurgitation. Note the large V waves in the PCWP with balloon inflation. (*From* Amin DA, Shah PK, Swan HJC: The Swan-Ganz catheter: Indications for insertion. J Crit Illness 1:54–61, 1986; with permission.)

benefit of preoperative PA catheter monitoring for assessment of hemodynamic function, adequacy of therapeutic intervention, and prognostic classification in elderly surgical patients.

PA catheters have been used for intracardiac electrocardiographic recording. Atrial, ventricular, and A-V sequential cardiac pacing can be achieved with PA catheters.[27] Recent catheter modifications providing for the determination of right ventricular ejection fraction are being evaluated. Clinical value and application of this measurement is yet to be determined.

SUMMARY

Since its introduction in 1970, the application for PA catheter monitoring has dramatically broadened. PA catheters provide the ability to obtain hemodynamic data for the assessment, monitoring, and therapeutic management of critically ill, high-risk surgical patients.

Because of the potential complications associated with PA catheter monitoring, numerous editorials and articles have questioned the procedure's risk-to-benefit ratio.[36,66,67] These articles address the insufficient availability of adequate outcome data or suggest no demonstrated benefit from PA monitoring. Subgroups of patients have been identified in whom the data obtained from PA monitoring altered the clinicians' assessment and management.[20,28,41,82] In spite of the study of Rao et al,[63] which implies that PA catheters can improve the mortality rate in critically ill patients, no scientific study of outcome has been able to confirm this impression.

If an adequate understanding of the limitations of PA monitoring does not exist, appropriate selection and implementation of therapy cannot occur. The problem is not as much the technology as it is the knowledge and expectations of the clinician. "Human" complications from inadequate understanding of the physiologic data is quite common. Reliance on the measured pressure is often misleading. The use of "absolute numbers" rather than trends or relative changes in the values monitored can compromise clinical assessment. Overzealous utilization and acceptance of any quantitative measurement without coordination with clinical judgment is fraught with failure.

REFERENCES

1. Amin DK, Shah PK, Swan HJC: The Swan-Ganz catheter: Insertion technique. J Crit Ill 1:38–45, 1986
2. Amin DK, Shah PK, Swan HJC: The Swan-Ganz catheter: Indications for insertion. J Crit Ill 1:54–61, 1986
3. Applefeld JJ, Caruthers TE, Renod J, et al: Assessment of the sterility of long-term cardiac catheterization using the thermodilution Swan-Ganz catheter. Chest 74:377–380, 1978
4. Armengol J, Man GCW, Balsys AJ, et al: Effects of respiratory cycle on cardiac output measurements: Reproducibility of data enhanced by timing of thermodilution injections in dogs. Crit Care Med 9:852–854, 1981
5. Baele PL, McMichan JC, Marsh MB, et al: Continuous monitoring of mixed venous oxygen saturation in critically ill patients. Anesth Analg 61:513–517, 1982
6. Band JD, Mahi DG: Infections caused by arterial catheters used for hemodynamic monitoring. Am J Med 67:735–741, 1979
7. Barash PG, Nardi D, Hammond G, et al: Catheter-induced pulmonary artery perforation, mechanisms, management and modifications. J Thorac Cardiovasc Surg 82:5–12, 1981
8. Beaupre PN, Cahalan MK, Kremer PF, et al: Does pulmonary artery occlusion pressure adequately reflect left ventricular filling during anesthesia and surgery. Anesthesiology 59:A3, 1983
9. Benumof JL: Anesthesia for Thoracic Surgery, ed 1. Philadelphia, W.B. Saunders, 1987
10. Benumof JL, Saidman LJ, Arkin DB, et al: Where do pulmonary artery catheters go intrathoracic distribution. Anesthesiology 46:336–338, 1977
11. Bernhardt LC, et al: Intravenous catheter embolization to pulmonary artery. Chest 57:329–332, 1970
12. Berryhill RE, Benumof JL: PEEP-induced discrepancy between pulmonary arterial wedge pressure and left atrial pressure. The influence of controlled vs. spontaneous ventilation and compliant vs. non-compliant lungs. Anesthesiology 46:383–386, 1979
13. Birman H, Hag A, Hew E, et al: Continuous monitoring of mixed venous oxygen saturation in hemodynamically unstable patients. Chest 85:753–756, 1984
14. Brown CQ: Inadvertent prolonged cannulation of the carotid artery. Anesth Analg 61:150–152, 1982
15. Carlile PV: Pitfalls in the interpretation of hemodynamic data. Prog Crit Care Med 2:69–86, 1985
16. Chapin JC, Downs JB, Douglas ME, et al: Lung expansion, airway pressure transmission and positive end-expiratory pressure. Arch Surg 114:1193–1197, 1979
17. Chastre J, Cornud F, Bouchama A, et al: Thrombosis as a complication of pulmonary artery catheterizations via the internal jugular vein. Prospective study by phlebography. N Engl J Med 306:278–281, 1982
18. Civetta JM, Gabel JC: Flow directed pulmonary artery catheterization: Indications and modifications of technique. Ann Surg 176:753–756, 1972
19. Civetta JM, Hudson-Civetta JA, Nelson LD, et al: Utility and efficacy of guidewire changes. Crit Care Med 15(a):380, 1987

20. Connors AF, McCaffree DR, Gray BA: Evaluation of right heart catheterization in the critically ill patient with acute myocardial infarction. N Engl J Med 308:263–267, 1983
21. Davies MJ, Cronin KD, Domainque E: Pulmonary artery catheterization. An assessment of risks and benefits in 220 surgical patients. Anesthes Intens Care 10:9–14, 1982
22. DeCampo T, Civetta JM: The effects of short-term discontinuation of high-level PEEP in patients with acute respiratory failure. Crit Care Med 7:47–49, 1979
23. Del Guercio LM, Cohn JD: Monitoring operative risk in the elderly. JAMA 243:1350–1355, 1980
24. Deren MM, Barash PG, Hammond GE, et al: Perforation of the pulmonary artery requiring pneumonectomy after the use of a flow-directed Swan-Ganz catheter. Thorax 34:550, 1979
25. Doblar DD, Hinkle JC, Fay ML, et al: Air embolism associated with pulmonary artery catheter introducer kit. Anesthesiology 56:307–309, 1982
26. Dongre SS, McAslan TC, Shin B: Selection of the source of mixed venous blood samples in severely traumatized patients. Anesth Analg 56:527–532, 1977
27. Donovan KL: Invasive monitoring and support of the circulation. Clin Anesth 3:909–953, 1985
28. Eisenberg PR, Jaffe AS, Schuster DP: Clinical evaluation compared to pulmonary artery catheterization in the hemodynamic assessment of critically ill patients. Crit Care Med 12:549–553, 1984
29. Enson Y, Wood JA, Mantaras NB, et al: The influence of heart rate on pulmonary arterial-left ventricular pressure relationships at end-diastole. Circulation 56:533–539, 1977
30. Falicov RE, Resnekov L: Relationship of pulmonary artery end-diastolic pressure to left ventricular end-diastolic and mean filling pressures in patients with and without left ventricular dysfunction. Circulation 42:65–73, 1970
31. Forrester JS, Diamond G, McHugh TJ, et al: Filling pressures in right and left sides of the heart in acute myocardial infarction. A reappraisal of central venous pressure monitoring. N Engl J Med 285:190–193, 1971
32. Forrester JS, Diamond GA, Swan HJC: Correlative classification of clinical and hemodynamic function after acute myocardial infarction. Am J Cardiol 39:137–145, 1977
33. Ganz W, Donoso R, Marcus H, et al: A new technique for measurement of cardiac output by thermodilution in man. Am J Cardiol 27:392–396, 1971
34. Gardner RM: Direct blood pressure measurement dynamic response requirements. Anesthesiology 54:227–236, 1981
35. Gardner RM, Bond EL, Clark JS: Safety and efficacy of continuous flush systems for arterial and pulmonary artery catheters. Ann Thorac Surg 23:534–538, 1977
36. Gore JM, Goldbert RJ, Spodick DH, et al: A community-wide assessment of the use of pulmonary artery catheters in patients with acute myocardial infarction. Chest 92:721–727, 1987
37. Hasan FM, Weiss WB, Bramain SS, et al: Influence of lung injury on pulmonary wedge-left atrial pressure correlation during positive end-expiratory pressure ventilation. Am Rev Respir Dis 131:246–250, 1985
38. Heard SO, Davis LF, Shevertz RJ, et al: Influence of sterile protective sleeves on the sterility of pulmonary artery catheters. Crit Care Med 15:499–502, 1987
39. Herbst CA: Indication, management and complications of percutaneous subclavian catheters. Arch Surg 113:1421–1425, 1978
40. Hoar PF, Wilson RM, Mangano DT, et al: Heparin bonding reduces thrombogenicity of pulmonary-artery catheters. N Engl J Med 305:993–995, 1981
41. Iberti TJ, Fisher LJ: A prospective study on the use of the pulmonary artery catheter in a medical intensive care unit, its effect on diagnosis and therapy. Crit Care Med 11:238, 1983
42. Jardin F, Farcot JC, Boisante L, et al: Influence of positive end-expiratory pressure on left ventricular performance. N Engl J Med 304:387–392, 1981
43. Kandel G, Aberman A: Mixed venous oxygen saturation; its role in the assessment of the critically ill patient. Arch Intern Med 143:1400–1402, 1983

44. Kaplan JA, Wells PH: Early diagnosis of myocardial ischemia using the pulmonary arterial catheter. Anesth Analg 60:789–793, 1981
45. Khalil KG, et al: Thoracic duct injury; a complication of jugular vein catheterization. JAMA 221:908–909, 1972
46. Khalil KG, et al: Thoracic duct injury; a complication of jugular vein catheterization. JAMA 221:908–909, 1972
47. Mangano DT: Monitoring pulmonary arterial pressure in coronary-artery disease. Anesthesiology 53:364–370, 1980
48. Marini JJ: Obtaining meaningful data from the Swan-Ganz catheter. Respir Care 30:572–585, 1988
49. Marini JJ: Hemodynamic monitoring with the pulmonary artery catheter. Crit Care Clin 2:551–572, 1986
50. Marini JJ, O'Quin R, Culver BH, et al: Estimation of transmural cardiac pressure during ventilation with PEEP. J Appl Physiol 53:384–391, 1982
51. Matthew EB, Vender JS: Comparison of thermodilution cardiac output measured by different computers. Crit Care Med 15:989, 1987
52. Mohsinifar Z, Goldbach P, Tashkin DP, et al: Relationship between O_2 delivery and O_2 consumption in the adult respiratory distress syndrome. Chest 84:267–271, 1983
53. Mohsinifar Z, Goldbach P, Tashkin DP, et al: Relationship between O_2 delivery and O_2 consumption in the adult respiratory distress syndrome. Chest 84:267–271, 1983
54. Morton BC: Basic equipment requirements for hemodynamic monitoring. Can Med Assoc J 121:879–885, 1979
55. Murray IP: Complications of invasive monitoring. Med Instrum 15:85–89, 1981
56. Obel I: Transient phrenic nerve paralysis following subclavian venipuncture. Anesthesiology 33:369–370, 1970
57. O'Quin R, Marini JJ: Pulmonary artery occlusion pressure: Clinical physiology, measurement, and interpretation. Am Rev Respir Dis 128:319–326, 1983
58. Pape LA, Haffajee CI, Markis JE, et al: Fatal pulmonary hemorrhage after use of the flow-directed balloon-tipped catheter. Ann Intern Med 90:344–347, 1979
59. Pepe PE, Marin JJ: Occult positive end-expiratory pressure in mechanically ventilated patients with airflow obstruction. Am Rev Respir Dis 126:166–170, 1982
60. Petty TL: Adult respiratory distress syndrome. Semin Respir Med 3:219–224, 1982
61. Puri VK, Carlson RW, Bander JT, et al: Complications of vascular catheterization in the critically ill. Crit Care Med 8:495–499, 1980
62. Rahimtoola SH, Loeb HS, Eshani A, et al: Relationship of pulmonary artery to left ventricular diastolic pressures in acute myocardial infarction. Circulation 46:283–290, 1972
63. Rao TLK, Jacobs HK, El-Etr AA: Reinfarction following anesthesia in patients with myocardial infarction. Anesthesiology 59:449–505, 1983
64. Räsänen J, Downs JB: Titration of continuous positive airway pressure by real-time dual oximetry. Crit Care Med 15(a):395, 1987
65. Riedinger MS, Shellock FG: Technical aspects of the thermodilution method for measuring cardiac output. Heart Lung 13:215–221, 1984
66. Robin ED: Death by pulmonary artery flow-directed catheter. Chest 92:727–731, 1987
67. Robin E: The cult of the Swan-Ganz catheter. Ann Intern Med 103:445–449, 1985
68. Rosenbaum L, Rosenbaum SH, Ashkanazi T, et al: Small amounts of hemoptysis as an early warning sign of pulmonary artery rupture by a pulmonary arterial catheter. Crit Care Med 9:319–320, 1981
69. Rowley KM, Clubb KS, Smith JW, et al: Right-sided infective endocarditis as a consequence of flow-directed pulmonary artery catheterization. N Engl J Med 311:1152–1156, 1984
70. Salmenpera M, Peltola K, Rosenberg P: Does prophylactic lidocaine control cardiac arrhythmias associated with pulmonary artery catheterization? Anesthesiology 56:210–212, 1982
71. Samii K, Conseiller C, Viars P: Central venous pressure and pulmonary wedge pressure. Arch Surg 111:1122–1125, 1976

72. Schwartz KV, Garcia FG: Entanglement of Swan-Ganz catheter around an intracardiac structure. JAMA 237:1198–1199, 1977
73. Schweiss JF: Mixed venous hemoglobin saturation: Theory and application. Int Anesthes Clin 25:113–136, 1987
74. Shah KB, Rao TK, Laughlin S, et al: A review of pulmonary artery catheterization in 6245 patients. Anesthesiology 61:271–275, 1984
75. Snyder JV, Powner DJ: Effects of mechanical ventilation on the measurement of cardiac output by thermodilution. Crit Care Med 10:677–682, 1982
76. Sprung CL, Pogen RG, Rozanski JJ, et al: Advanced ventricular arrhythmias during Swan-Ganz catheterization of the critically ill. Am J Med 72:203–208, 1982
77. Stetz CW, Miller RG, Kelly GE, et al: Reliability of the thermodilution method in the determination of cardiac output in clinical practice. Am Rev Respir Dis 126:1001–1004, 1982
78. Stoller JK, Herbst TJ, Hurford W, et al: Spuriously high output from injecting thermal indicator through an ensheathed port. Crit Care Med 14:1064–1065, 1986
79. Swan HJC: Central venous pressure monitoring is an outmoded procedure of limited practical value. *In* Ingelfinger FJ, Ebert RV, Finland M, et al (eds): Controversies in Internal Medicine. Philadelphia, W.B. Saunders, 1974, pp 185–193
80. Swan HJC, Ganz W: Hemodynamic measurements in clinical practice: A decade in review. J Am Coll Cardiol 1:103–113, 1983
81. Tenney SM: A theoretical analysis of the relationship between venous blood and mean tissue oxygen pressures. Respir Physiol 20:283–296, 1974
82. Tuchschmidt J, Sharma OMP: Impact of hemodynamic monitoring in a medical intensive care unit. Crit Care Med 15:840–843, 1987
83. Voukydis PC, Cohen SI: Catheter-induced arrhythmias. Am Heart J 88:588–592, 1974
84. Weil MH, Henning RJ: New concepts in diagnosis and fluid treatment in circulatory shock. Anesth Analg 58:124–132, 1979
85. West JB, Dollery CT, Naimark A: Distribution of blood flow in isolated lung; relation to vascular and alveolar pressures. J Appl Physiol 19:713–724, 1964

Intensive Care
Evanston Hospital
2650 Ridge Avenue
Evanston, IL 60201

0889-8537/88 $0.00 + .20

Perioperative Echocardiography

*John R. Slavik, MD**

Recently, noninvasive imaging modalities have undergone considerable evolution. Ultrasound examination of the heart has benefited from continued advances in electronic manipulation of acquired data. The result has been the ability to produce real-time images of the heart in which anatomy and function can be easily defined. The use of echocardiography to evaluate patients with cardiovascular disease during the preoperative period has now become commonplace. With the introduction of ultrasound transducers mounted on a gastroscope, continuous monitoring of cardiovascular performance of surgical patients is now available in the operating room.

ULTRASOUND

Sound with a frequency greater than 20,000 cycles per second is ultrasound. However, for medical diagnostic purposes, the soundwave frequencies employed are between 2.25 and 7.5 million cycles per second (MHz). These soundwaves are produced by a piezoelectric crystal embedded in a transducer device. The transducer serves as both transmitter and receiver (Fig. 1). The velocity of sound in human soft tissues at 37°C is 1540 meters per second. Imaging with this technique is possible because the soundwaves are reflected, refracted, or transmitted at tissue interfaces with differing acoustic properties. For example, considerable reflection occurs at the ventricular endocardium because of a difference between the acoustic properties of myocardium and blood. The time difference between sound emission and return from the reflecting surface produces a measure of distance from the transducer. The greater the fraction of the reflected sound, the brighter will be its representation on the display screen. Image quality depends on the frequency of the ultrasound employed. The higher the frequency the better the image definition. Unfortunately, higher frequency ultrasound is more easily attenuated. Therefore,

---

*Assistant Professor, Department of Anesthesiology, Yale University School of Medicine, Yale-New Haven Hospital, New Haven, Connecticut

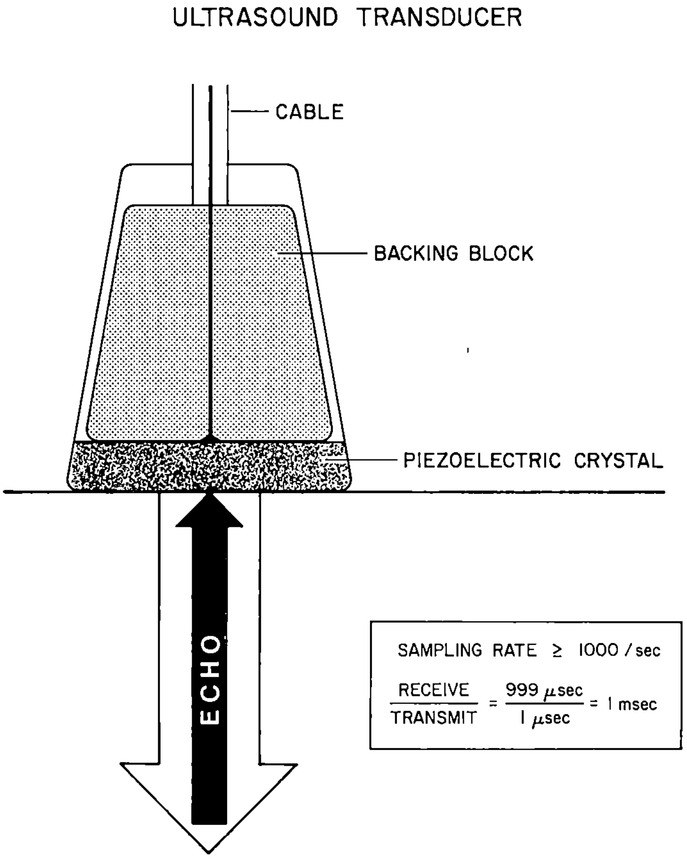

ULTRASOUND TRANSDUCER
CABLE
BACKING BLOCK
PIEZOELECTRIC CRYSTAL
ECHO
SAMPLING RATE ≥ 1000 /sec
$\frac{\text{RECEIVE}}{\text{TRANSMIT}} = \frac{999\ \mu\text{sec}}{1\ \mu\text{sec}} = 1\ \text{msec}$

Figure 1. Ultrasound transducer. A typical M-mode transducer samples at rates of 1000 images per second and allows analysis of rapidly moving structures, such as cardiac valves. A two-dimensional echo transducer is comparable except sampling rates are much slower (30 images per second).

in order to image deeper structures, a lower frequency may be needed. In practice, most ultrasound transducers are 3.5 to 5 MHz.[3,8]

ECHOCARDIOGRAPHY

The ultrasound examination of the heart uses one of two techniques: M-mode (motion mode) and two-dimensional (cross-sectional) echocardiography (Fig. 2). With M-mode a one-dimensional image, representing an "ice-pick" view of the heart, is produced. M-mode examination is gradually being supplanted by two-dimensional echocardiography. However, since M-mode sampling rates are about 1000 images per second, it is still employed to provide information on rapidly moving cardiac structures such as heart valves. Two-dimensional echocardiographic analysis produces an anatomic slice that is more

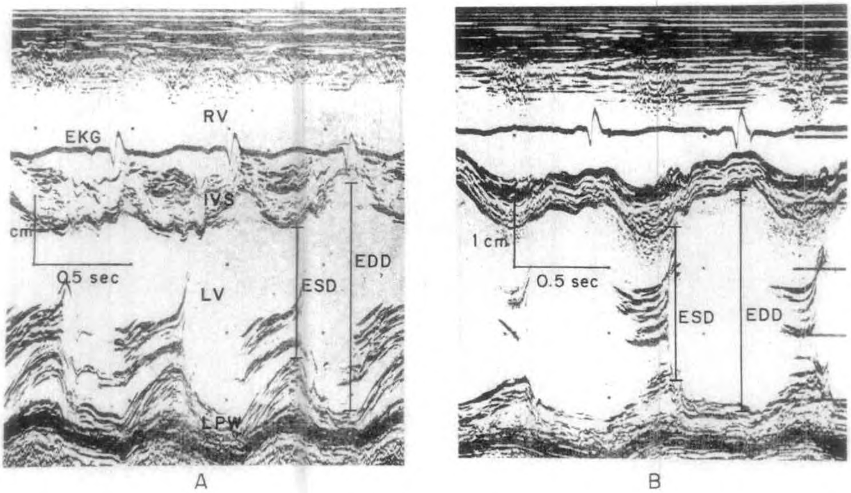


Figure 2. Example of M-mode echocardiograms obtained during a clinical study that examined the effects of halothane anesthesia in children. (*A*) Patient awake prior to study. (*B*) Following administration of halothane (2 per cent). End-systolic dimension is reduced suggesting decreased contractility. RV = right ventricle, LV = left ventricle, ESD = end-systolic dimension, EDD = end-diastolic dimension, EKG = electrocardiogram. (*From* Barash PG, et al: Ventricular function in children during halothane anesthesia: An echocardiographic evaluation. Anesthesiology 49:79–85, 1978; with permission.)

easily recognized and interpreted. The ultrasound sampling rates in the two-dimensional mode are much lower, about 30 frames per second, but the ability to recognize anatomic landmarks is considered advantageous. Considerable training is required to recognize the unfamiliar patterns generated by the M-mode technique, while two-dimensional echocardiograms have almost immediate significance to an untrained observer.

EXAMINATION

Precordial echocardiographic examination is based on the presence of several "windows" through which visualization of the heart is possible. Since ultrasound is not transmitted through air or bone, imaging through the lung, sternum, or ribs is not feasible. Thus, windows exist wherever ultrasound may reach the heart without encountering lung or bone. Views are usually obtained through the parasternal, apical, subcostal, and suprasternal windows. Some patients, particularly those with increased lung volumes, may be difficult to image adequately transthoracically. In contrast, high-quality images can be obtained from an ultrasound transducer tipped gastroscope properly positioned in the esophagus. Schluter et al[22] initially reported the use of transesophageal echocardiography (TEE) to examine such patients. Six views were described using TEE. These are the aortic valve view, the mitral valve view, the left ventricular (LV) short-axis view, the apical view, the biatrial view, and the pulmonary view (Fig. 3). The goal of examination is to gain as much information concerning anatomy and function as possible. Sizes of cardiac chambers can be readily measured, and global and regional contraction patterns can be observed.

ANALYSIS OF GLOBAL VENTRICULAR FUNCTION

Monitoring of patients is undertaken either to prevent the occurrence of untoward complications or to treat them appropriately. With reference to the cardiovascular system, this currently entails the placement of invasive catheters to assess hemodynamic function, that is, systemic and pulmonary arterial cannulation. This allows both pressure measurements as well as cardiac output determinations. However, under certain clinical circumstances, changes in ventricular filling pressures may not accurately reflect changes in actual ventricular volumes. Thus, a measure of ventricular volume will more accurately predict hemodynamic improvement or deterioration. Echocardiography offers a route to these measurements.

USE OF M-MODE ECHOCARDIOGRAPHY IN EVALUATING GLOBAL VENTRICULAR FUNCTION

LV linear dimensions may be determined employing M-mode analysis. LV volumes may then be estimated *assuming* that the LV is an ellipsoid of revolution, that it contracts symmetrically along its major axis, and that the echo dimension used is the lateral minor axis at its maximal circumference (short axis at the level of the mitral valve). Ejection fraction (EF) may be determined after volume calculations are made. Shortening fraction and mean velocity of circumferential fiber shortening (V_{cf}) can also be calculated using the information obtained previously. Shortening fraction is defined as the difference between end-diastolic and end-systolic linear dimensions divided by the end-diastolic dimension. V_{cf} is the shortening fraction divided by the left ventricular ejection time (LVET). Systolic time intervals are also determined easily by M-mode echocardiography. The pre-ejection period (PEP) is defined as the interval between the QRS complex of a simultaneously recorded ECG and aortic valve cusp opening. LVET is defined as the interval between aortic valve cusp opening and closure. These measurements then are used to evaluate ventricular performance: end-diastolic volumes are a measure of preload, EF, shortening fraction, mean V_{cf} are measures of contractility, and PEP and LVET are indices of vascular resistance.[15]

To determine the effects of increasing halothane concentrations

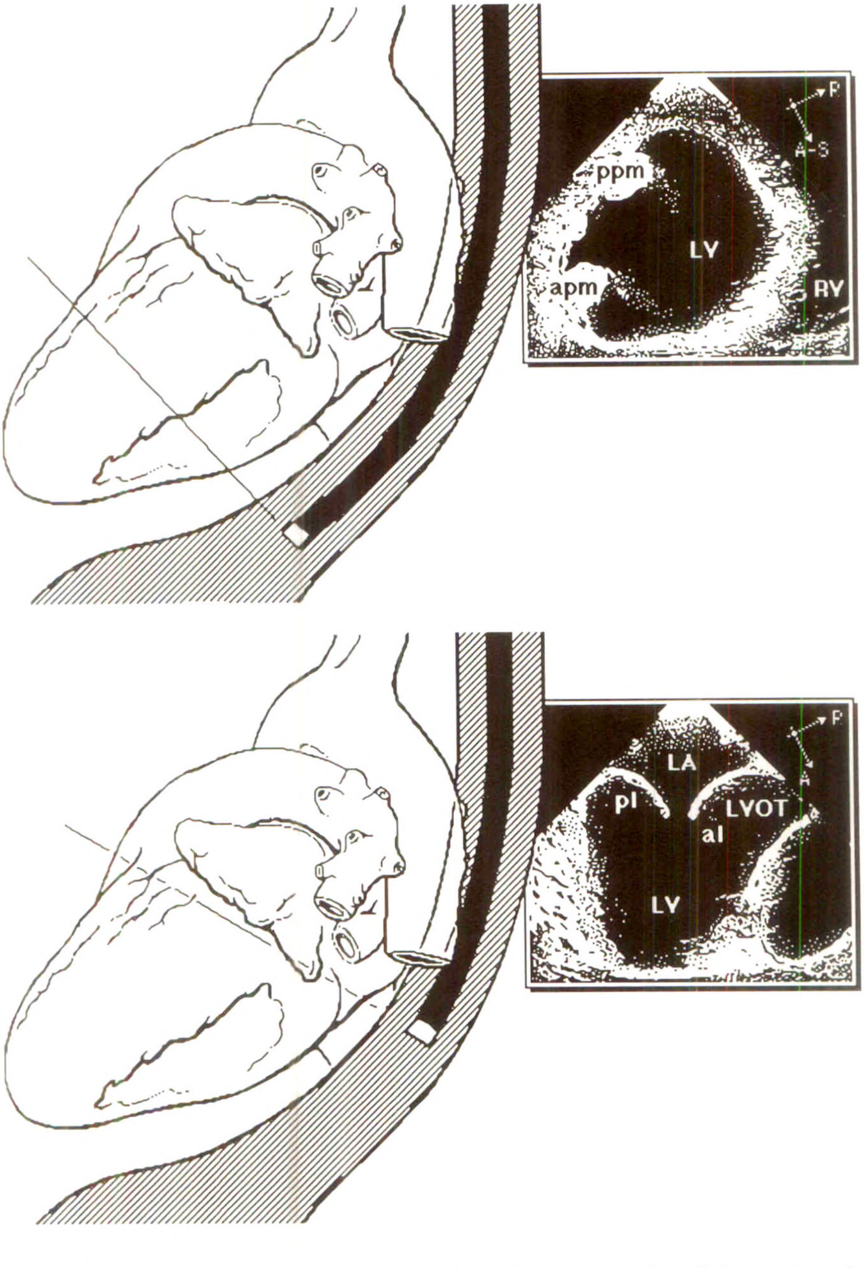


Figure 3. Computer-generated images demonstrating position of the transesophageal echo transducer and the corresponding images for the LV short axis (*A*) and mitral valve views (*B*). Al = anterior leaflet, pl = post-leaflet (mitral valve), APM = anterior papillary muscle, PPM = post-papillary muscle, LA = left atrium, LV = left ventricle, LVOT = LV outflow tract, RV = right ventricle. (Courtesy of Pat Lynch and Carl Jaffe, MD, Yale Department of Diagnostic Imaging and Medical Illustration.)

on the ventricular function of 13 healthy children, Barash et al[2] used M-mode echocardiography to obtain a number of parameters described previously (Fig. 2). Cardiac output determinations (the product of stroke volume and heart rate) revealed that dose-related depression was present and that atropine could reverse this effect. However, V_{cf} exhibited the greatest dose-related depression and did not fully recover following atropine administration. This suggested continued myocardial depression despite return of the cardiac output to nearly normal values (following atropine). Although no change in the left ventricular end-diastolic volume (LVEDV) occurred, EF decreased and the PEP/LVET ratio increased during halothane administration. Again, this suggests decreased systolic function.

Rathod et al[19] studied the effects on ventricular performance of anesthesia induction with either of two inhalation agents in 20 healthy adults. Halothane, at an end-tidal concentration of 0.93 per cent, was compared with enflurane, 2.4 per cent inspired. Exposure to halothane resulted in a decrease in arterial pressure, fractional shortening, and mean V_{cf}, while no change was observed in heart rate, central venous pressure, or left atrial dimensions. Enflurane caused no change in fractional shortening and mean V_{cf}, but a decrease in arterial pressure and an increase in heart rate were noted. No change was observed in central venous pressure or left atrial dimensions with enflurane. The decreased ventricular function with halothane is again obvious, but enflurane appeared not to decrease myocardial function. However, an increase in heart rate and a decrease in arterial pressure would be expected to result in an increase in indices of contractility. Since this did not occur, it appears that the negative inotropic effects of enflurane were masked.

Wolf et al[31] compared the cardiovascular effects of isoflurane with halothane using M-mode echocardiography in children. Two equipotent anesthetic concentrations were selected to obtain echocardiographic measurements. Left ventricular end-diastolic and end-systolic dimensions were not altered in either group. Halothane caused decreases in the shortening fractions and mean V_{cf}, and an increase in the PEP/LVET ratio, all suggesting considerable myocardial depression. Isoflurane did not alter shortening fraction or mean V_{cf}, and the PEP/LVET ratio decreased. Heart rate and blood pressure decreased similarly in both groups. These results suggest greater cardiac reserve with isoflurane, a finding that would not be appreciated with analysis of blood pressure and heart rate only.

The initial use of transesophageal echocardiography in the operating room employed M-mode methods. Matsumoto et al[14] evaluated its use in 21 patients undergoing valvular or coronary heart surgery. They found that LV dimensions measured with the transesophageal approach correlated nicely with those measured by precordial methods. LV volumes at end-diastole and end-systole were determined and cardiaac outputs were calculated. These correlated reasonably with outputs by dye dilution. Those patients who underwent valve replacement demonstrated a decrease in LV dimensions, V_{cf}, and EF after cardiopulmonary bypass. No significant change in cardiac output, EF, or V_{cf} was observed in patients who underwent coronary bypass grafting. A decrease in LV dimensions was documented in both patient groups after sternal closure, suggesting a restriction to LV expansion.

Since volume determinations by M-mode echocardiography are calculated from a measurement in a single dimension, any error made in obtaining it would be magnified in the subsequent calculations. This is a particular problem in patients with abnormally shaped ventricles and those with regional contraction abnormalities. Attempting to make generalizations concerning global ventricular function by observing the contraction pattern of two myocardial segments along a "line-of-site" can be misleading. Thus, two-dimensional echocardiography, in which a cross section of the heart is examined, is gaining favor because additional information is obtained by observing the contraction pattern of a circumferential image.

USE OF TWO-DIMENSIONAL ECHOCARDIOGRAPHY IN EVALUATING GLOBAL VENTRICULAR FUNCTION

LV *areas* may be measured using two-dimensional echocardiography. This entails tracing the end-systolic and end-diastolic endocardial borders and then determining the area inscribed. End-diastolic area provides a relative estimate of LV volume. Two parameters of global ventricular function that may be calculated from these measurements are the fractional area change and the per cent circumferential shortening. Fractional area change (or EF area) is defined as the difference between end-diastolic and end-systolic areas divided by the end-diastolic area. Per cent circumferential shortening is the difference between end-diastolic and end-systolic circumferences divided by the end-diastolic circumference. Since these calculations require a considerable amount of time, the results will not be immediately available to guide the clinician. Fortunately, an experienced observer may make qualitative assessments concerning ventricular size and function by careful observation of the video screen.

Abel et al[1] used two-dimensional TEE to monitor 11 patients who were undergoing coronary bypass grafting. Short-axis (cross-sectional) images were obtained at the midpapillary muscle level. Global left ventricular function was assessed by determining the fractional area change. These measurements were shown to have good intraobserver reproducibility. Thys et al[29] examined 12 patients with good ventricular function undergoing coronary bypass grafting before and after cardiopulmonary bypass. Two-dimensional short-axis views of the LV were obtained by *epicardial* placement of a 5 MHz transducer and the derived measurements were compared with concurrently acquired invasive hemodynamic data. End-systolic areas and end-diastolic areas were determined, and then ventricular volumes were calculated using a modified ellipsoid model. This allowed determination of stroke volume and cardiac output from the echocardiographic data. In addition, ventricular diameter and wall thickness were measured at end-systole to determine wall stress. Cardiac output, as determined by thermodilution, correlated well with that calculated from the echo data. The pulmonary capillary wedge pressure (PCWP), the conventional index of LV preload, correlated poorly with the end-diastolic area or the derived end-distolic volume ($V = (SA)^{3/2}(36 + SA)/(12 + SA)$ where SA = short-axis area). There was a strong correlation between the cardiac output, as determined by echocardiography or by thermodilution, and the end-diastolic area or volume. However, no correlation was noted between PCWP and cardiac output as calculated either by the echo information or by the thermodilution technique. It is clear from this information that end-diastolic size is the best predictor of cardiac output, and that the PCWP does not always reflect actual changes in ventricular volume. If this hypothesis is correct, the Frank-Starling principle cannot be uniformly applied in situations where LV compliance is altered (for example, myocardial ischemia). Under these circumstances, only a measure of ventricular size (either area or volume) can assist in maximizing ventricular preload and cardiac output. Measurements obtained from two-dimensional TEE have been shown to correlate well with those obtained from on-heart transducers by Konstadt et al.[11] Thus, anesthesiologists will be able to gather the same information as described by Thys et al without interruption of the surgical procedure.

Murray et al[17] employed precordial two-dimensional echocardiography and pulsed Doppler (see article by LaMantia in this issue) to examine the effects of halothane and isoflurane on cardiac function in 20 infants and children. Measurements were taken prior to inhalation induction, at 0.75, 1.00, and 1.25 MAC, and after a 15 ml per kg bolus of lactated Ringer's solution. Ventilation via mask was controlled in each patient during the examination. Left ventricular volume determinatins were made using information from both the short-axis (cross-sectional) and the long-axis views. Cardiac outputs were determined using the Doppler technique, which measured blood flow velocity across the pulmonary valve. The results reveal that halothane and isoflurane depress cardiac function similarly. Mean arterial pressure, cardiac index, stroke volume index, and EF decreased and LV end-diastolic and end-systolic volumes increased during the study. After the volume load, those patients receiving halothane showed further decreases in EF and stroke volume index, but those maintained on isoflurane demonstrated increases in both EF and stroke volume index. This may indicate greater cardiovascular reserve in infants and children anesthetized with isoflurane.

USES OF TWO-DIMENSIONAL ECHOCARDIOGRAPHY IN EVALUATING REGIONAL VENTRICULAR FUNCTION

In 1935, in a now classic set of animal experiments, Tennant and Wiggers[28] observed the response of ventricular muscle when the coronary artery supplying it was ligated. In dogs anesthetized with morphine and sodium barbital, myographic recordings were obtained from ventricular muscle before and after the coronary artery supplying the area was ligated. Contraction disturbances occurred in seconds after coronary blood flow ceased. Initially, the deprived segments showed decreasing contractile function (hypokinesis). This was followed by a period in which the muscle did not contract during systole at all (akinesis). Finally, the ventricular muscle was noted to bulge outward during systole (dyskinesis). These alterations developed over a period of about 1 minute, and functional recovery was possible if the ischemic time was not excessive. These experimental observations form the basis of modern echocardiographic evaluation of myocardial ischemia.

In the interim, a number of clinical studies have found echocardiography to be very sensitive and specific in detecting coronary artery disease. Horowitz et al[10] studied patients presenting to an emergency room with acute chest pain. Two-dimensional echocardiograms were obtained in 65 patients (81 per cent) and were inadequate for analysis in the rest. Thirty-three of these had clinical evidence of acute infarction (subsequent ECG changes and CPK elevation), 18 of which had nondiagnostic electrocardiographic changes at initial presentation. Thirty-one of the 33 patients with acute infarctions had regional wall motion abnormalities on the initial two-dimensional echo examination. Almost a third of patients with regional wall motion abnormalities on initial presentation suffered a serious cardiac complication following admission to the hospital. Thus, two-dimensional echocardiography not only identified those patients with acute ischemia, but defined a high-risk group who are likely to have important complications during the hospital course.

Limacher et al[13] used two-dimensional echocardiography to detect regional wall motion abnormalities and EF immediately after stress testing. Those patients later shown to have normal coronary arteries demonstrated an increase in EF and no wall motion abnormalities after maximal exercise. Those subsequently demonstrated to have coronary artery disease revealed decreases in EF and a significant fall in a wall motion score index postexercise. A comparison was also made between two-dimensional echocardiography and radionuclide ventriculography. Two-dimensional echocardiography had a greater sensitivity and specificity for detection of coronary artery disease.

With the availability of TEE, clinical studies in patients with coronary artery disease undergoing stressful operative procedures have appeared. Two-dimensional echocardiography has proved to be an excellent indicator of myocardial ischemia. Roizen et al[21] studied patients undergoing aortic reconstructive surgery with two-dimensional TEE. They were separated into three groups based on the site of application of the aortic cross-clamp. Those patients undergoing supraceliac aortic clamping showed major increases in left ventricular end-diastolic and end-systolic area, decreases in the EF area, and frequent wall motion abnormalities. Clamping at the suprarenal-infraceliac level caused similar but smaller changes; and clamping at infrarenal levels caused minimal cardiovascular changes. Despite the fact that vasodilators or anesthetics were used to maintain intravascular pressures at peroperative levels, changes suggesting the presence of myocardial ischemia were detected by two-dimensional TEE. These changes were not appreciated using traditional measures of cardiovascular performance, that is, invasive monitoring with a pulmonary artery catheter. The two-dimensional TEE allowed early detection of myocardial ischemia when it is likely to be most amendable to treatment.

Smith et al[24] compared the incidence of myocardial ischemia as detected by two-dimensional TEE and surface electrocardiography during anesthesia and surgery in high-risk patients. Fifty patients were studied. Twenty-four of these developed acute regional wall motion abnormalities during operation, but only six (6/24) had new ST-segment changes on the ECG. All six patients with ECG changes also showed ventricular wall motion abnormalities, and three of these patients developed the regional wall contraction abnormalities prior to the ECG changes. Of the three patients who suffered intraoperative myocardial infarction, only one had ST-segment changes while all had persistent regional contraction abnormalities observed with two-dimensional TEE. Thus, it is clear that two-dimensional TEE is a more sensitive detector of myocardial ischemia than the ECG.

Two-dimensional TEE is also being employed to examine the effects of pharmacologic agents on the heart. Both nitrous oxide and isoflurane have recently been implicated in the production of myocardial ischemia in models of ischemic heart disease as well as in man. Philbin et al[18] in a canine model of acute coronary constriction demonstrated postsystolic shortening when nitrous oxide was added to a narcotic-based anesthetic. These changes occurred consistently and were not always reversible. However, Cahalan et al[4] studied patients with coronary artery disease anesthetized with fentanyl who were about to undergo coronary bypass grafting. Patients were exposed to nitrous oxide and nitrogen in sequence and observed for wall motion abnormalities with two-dimensional TEE and for ischemic ECG changes. Eighteen patients were studied and none developed regional wall motion abnormalities when exposed to nitrous oxide. Slavik et al[25] studied patients with coronary artery disease who were anesthetized with sufentanil during the precardiopulmonary bypass period. Using two-dimensional TEE, they were also unable to demonstrate any regional contraction abnormalities after exposure to both nitrous oxide or nitrogen in a randomized sequence (Fig. 4). Moffitt et al[16] anesthetized patients with coronary artery disease who were about to undergo bypass grafting with isoflurane. They found evidence of redistribution of myocardial blood flow (coronary steal phenomenon). LaMantia et al,[12] in patients who were anesthetized with sufentanil, examined the response of the LV by two-dimensional TEE when a modest dose of isoflurane was added to the inspired gases (0.6 per cent end-tidal). Their results showed stable global LV function as determined by area EF, and regional function was not

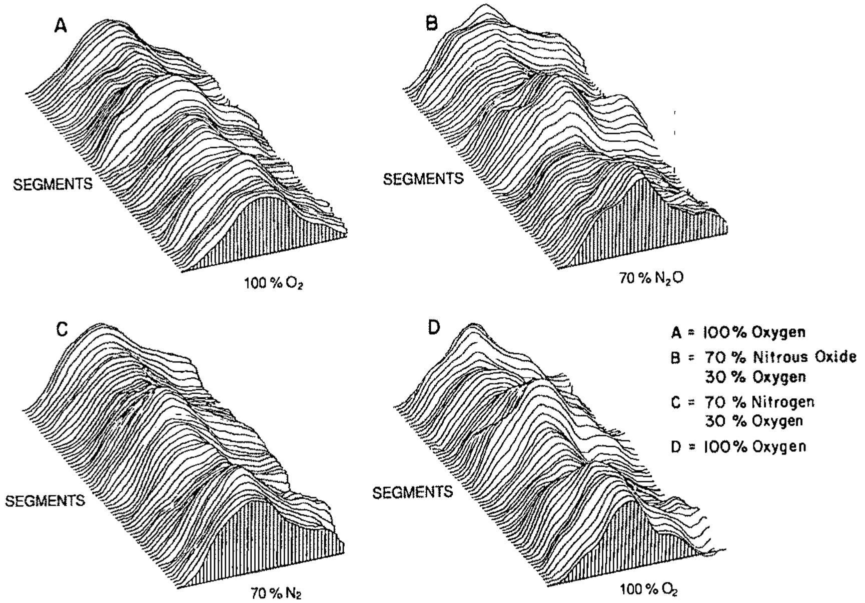


Figure 4. Computer analysis of LV endocardial motion from each of four study phases during which patients were randomly exposed to nitrous oxide, nitrogen, and 100 per cent oxygen. No regional wall motion abnormalities could be demonstrated. Each LV cross section is divided into 64 equiangular segments to facilitate analysis. These are then plotted against time for a cardiac cycle. Rises in contour indicate inward endocardial wall motion. (*From* Slavik JR, LaMantia KR, Kopriva CJ, et al: Does nitrous oxide cause regional wall motion abnormalities in patients with coronary artery disease? An evaluation by two-dimensional transesophageal echocardiography. Anesth Analg 67:695–700, 1988; with permission.)

disturbed. This suggests that isoflurane, used in low concentration as an adjunct to a narcotic-based anesthetic, does not result in coronary steal phenomenon.

USE OF ECHOCARDIOGRAPHY TO DETECT INTRACARDIAC AIR

Because of differing acoustical properties between air and blood, minute amounts of air may be easily detected inside a cardiac chamber. When air enters a cardiac chamber, a bright speckled pattern is observed on the video screen in that chamber. This has monitoring implications for those surgical procedures in which introduction of air into the vascular system may occur. These include craniotomy performed in the sitting position and open heart operations, such as valve replacements. Furuya et al[9] used transesophageal M-mode echocardiography to determine the quantity of air that could be detected by this technique versus conventional precordial Doppler. In a canine model, TEE detected 0.02 ml per kg of air injected intravenously, while the precordial Doppler signal did not change until a bolus of 0.05 mg per kg was administered. When air was introduced into the left ventricle, it was detected in the aorta by TEE after only 0.001 ml per kg was given. In a separate clinical study, five of six patients undergoing sitting craniotomy were found to have had venous air embolism. TEE is at least as sensitive as precordial Doppler, and it offers the advantage of being able to localize air to a specific cardiac chamber. Not only may venous air embolism be detected, but if paradoxical embolization occurs, it can be observed easily. Cucchiara et al[6] used two-dimensional TEE to test its sensitivity in the detection of intracardiac air in the neurosurgical environment. Nine of 15 patients studied had air embolism detected by both precordial Doppler and two-dimensional TEE. In two patients, data from the precordial Doppler were questionable, but the two-dimensional TEE showed numerous air bubbles. In addition, one patient had a paradoxical air embolism detected by two-dimensional TEE. Air was easily seen passing from the right atrium to left atrium and from there to the LV and the aorta.

The inability to evacuate all air introduced in the heart during an open cardiac surgical procedure can result in devastating consequences for the patient. Echocardiography also offers the ability to detect air under these operative circumstances. Duff et al[7] placed dogs on cardiopulmonary bypass and fibrillated the heart. Various amounts of air were then injected and echocardiographic recordings were made. Two-thirds milliliter of air was detected with a 95 per cent accuracy. Rodigas et al[20] used on-heart echocardiographic transducers to determine the prevalence and clinical effects of residual air in the LV at the conclusion of cardiac surgery. Residual microbubbles were detected in 39 of 79 patients (49 per cent). The presence of the microbubbles was most closely related to valve surgery in which the left atrium or aorta was opened. No patient had a neurologic complication in the postoperative period.

USE OF ECHOCARDIOGRAPHY TO EVALUATE PATIENTS FOR HEART SURGERY

Previously, all patients who were to undergo open heart procedures were evaluated invasively by cardiac catheterization. As proper preoperative medical therapy and surgical intervention depend on accurate assessment of pathologic anatomy and physiology, this approach was deemed necessary. Catheterization of the heart and angiocardiography are not without risk.[26] However, with the appearance of two-dimensional echocardiography to define anatomy and pulsed Doppler echocardiography to evaluate physiology, cardiac catheterization may be avoided. St. John-Sutton et al[27] followed 305 patients who underwent valve replacement surgery. Of these, 184 had clinical findings confirmed by echocardiography and underwent operation without preoperative cardiac catheterization. Fifty-nine underwent catheterization because of persistent doubt about the severity of the valvular lesion, the possibility of severe coronary artery disease, or discordance between the clinical and echocardiographic data. Sixty-two additional patients were referred with catheterization data already completed. The preoperative diagnosis was confirmed in all patients; operative mortality and 2-year survival were the same in all three groups. Similar results have been published in the evaluation of patients with suspected atrial septal defects[23] and in infants with cyanotic heart disease in preparation for Blalock-Taussig shunt operations.[30] Routine catheterization before cardiac surgical intervention may become uncommon in the near future as a result of continued experience with echocardiographic techniques. Of course, catheterization will be required in patients with coronary artery disease to determine the sites of occlusive disease, and in circumstances when clinical and echocardiographic data do not complement one another.

SUMMARY

Echocardiography offers several advantages over current monitoring techniques. Qualitative changes in ventricular chamber size can be followed during operation, and quantitative assessment can be accomplished at a later time by review of the recorded data. This gives the observer a more precise measure of LV preload. Regional changes in LV function may also be observed.[5] These have been shown to be sensitive and specific indicators of myocardial ischemia, and in many cases, appear before changes in the ECG. Echocardiographic techniques may also be used to evaluate the cardiovascular effects of pharmacologic agents, including anesthetics. Intracardiac air is reliably detected by echocardiography. Further, it may be localized within the heart, which is an advantage over precordial Doppler ultrasound monitoring in patients undergoing procedures with high probability of venous air embolism. Lastly, echocardiography is assuming a more important role in the preoperative assessment of patients for cardiac surgery, and under certain circumstances, may obviate the need for cardiac catheterization.

REFERENCES

1. Abel MD, Nishimura RA, Callahan MJ, et al: Evaluation of intraoperative transesophageal two-dimensional echocardiography. Anesthesiology 66:64, 1987
2. Barash PG, Glanz S, Katz JD, et al: Ventricular function in children during halothane anesthesia. Anesthesiology 49:79, 1978
3. Cahalan MK, Litt L, Botvinick EH, et al: Advances in non-invasive cardiovascular imaging: Implications for the anesthesiologist. Anesthesiology 66:356, 1987
4. Cahalan MK, Prakash O, Rulf ENR, et al: Addition of nitrous oxide to fentanyl anesthesia does not induce myocardial ischemia in patients with ischemic heart disease. Anesthesiology 67:925, 1987
5. Clements FM, deBruijn NP: Perioperative evaluation of regional wall motion by transesophageal two-dimensional echocardiography. Anesth Analg 66:249–261, 1987
6. Cucchiara RF, Nugent M, Seward JB, et al: Air embolism in upright neurosurgical

patients: Detection and localization by two-dimensional transesophageal echocardiography. Anesthesiology 60:353, 1984

7. Duff HJ, Buda AJJ, Kramer R, et al: Detection of entrapped intracardiac air with intraoperative echocardiography. Am J Cardiol 50:255, 1982
8. Feigenbaum H: Echocardiography, ed. 4. Philadelphia, Lea & Febiger, 1986
9. Furuya H, Takao S, Okumura F, et al: Detection of air embolism by transesophageal echocardiography. Anesthesiology 58:124, 1983
10. Horowitz RS, Morganroth J, Parrotto C, et al: Immediate diagnosis of acute myocardial infarction by two-dimensional echocardiography. Circulation 65:323, 1982
11. Konstadt SN, Thys DM, Mindich BP, et al: Validation of quantitative intraoperative transesophageal echocardiography. Anesthesiology 65:418, 1986
12. LaMantia KR, Acampora GA, Prokop EK, et al: Does isoflurane induce myocardial ischemia? An echocardiographic evaluation [abstract]. Anesthesiology 67:A586, 1987
13. Limacher MC, Quinones MA, Poliner LR, et al: Detection of coronary artery disease with exercise two-dimensional echocardiography. Description of a clinically applicable method and comparison with radionuclide ventriculography. Circulation 67:1211, 1983
14. Matsumoto M, Oka Y, Strom J, et al: Application of transesophageal echocardiography to continuous intraoperative monitoring of left ventricular performance. Am J Cardiol 46:95, 1980
15. Meyer RA: Echocardiography—Application in assessing cardiac performance in clinical care. Anesthesiology 49:71, 1978
16. Moffitt EA, Barker RA, Glenn JJ, et al: Myocardial metabolism and hemodynamic responses with isoflurane anesthesia for coronary arterial surgery. Anesth Analg 65:53, 1986
17. Murray D, Vandewalker G, Matherne GP, et al: Pulsed Doppler and two-dimensional echocardiography: Comparison of halothane and isoflurane on cardiac function in infants and small children. Anesthesiology 67:211, 1987
18. Philbin DM, Foex P, Drummond G, et al: Post-systolic shortening of canine left ventricle supplied by a stenotic coronary artery when nitrous oxide is added in the presence of narcotics. Anesthesiology 62:166, 1985
19. Rathod R, Jacobs HK, Kramer NE, et al: Echocardiographic assessment of ventricular performance following induction with two anesthetics. Anesthesiology 49:86, 1978
20. Rodigas PC, Meyer FJ, Hassler GB, et al: Intraoperative 2-dimensional echocardiography: Ejection of microbubbles from the left ventricle after cardiac surgery. Am J Cardiol 50:1130, 1982
21. Roizen MF, Beaupre RN, Alpert RA, et al: Monitoring with two-dimensional echocardiography. Comparison of myocardial function in patients undergoing supraceliac, suprarenal-infraceliac, or intrarenal aortic occlusion. J Vasc Surg 1:300, 1984
22. Schluter M, Hinrichs A, Wolfgang T, et al: Transesophageal two-dimensional echocardiography: Comparison of ultrasonic and anatomic sections. Am J Cardiol 53:1173, 1984
23. Shub C, Tajik AJ, Seward JB, et al: Surgical repair of uncomplicated atrial septal defect without "routine" preoperative cardiac catheterization. J Am Coll Cardiol 6:49, 1985
24. Smith JS, Cahalan MK, Benefiel DJ, et al: Intraoperative detection of myocardial ischemia in high-risk patients: Electrocardiography versus two-dimensional transesophageal echocardiography. Circulation 72:1015, 1985
25. Slavik JR, LaMantia KR, Kopriva CJ, et al: Does nitrous oxide cause regional wall motion abnormalities in patients with coronary artery disease? An evaluation by two-dimensional transesophageal echocardiography. Anesth Analg 67:695–700, 1988
26. Stanger P, Heymann MA, Tarnoff H, et al: Complications of cardiac catheterization of neonates, infants, and children. A three-year study. Circulation 50:595, 1974
27. St. John Sutton MG, St. John Sutton M, Oldershaw P, et al: Valve replacement without preoperative cardiac catheterization. N Engl J Med 305:1233, 1981

28. Tennant R, Wiggers CJ: The effect of coronary occlusion on myocardial contraction. Am J Physiol 112:351, 1935
29. Thys DM, Hillel Z, Goldman ME, et al: A comparison of hemodynamic indices derived by invasive monitoring and two-dimensional echocardiography. Anesthesiology 67:630, 1987
30. Ueda K, Nojima K, Saito A, et al: Modified Blalock-Taussig shunt operation without cardiac catheterization: Two-dimensional echocardiographic peroperative assessment in cyanotic infants. Am J Cardiol 54:1296, 1984
31. Wolf WJ, Neal MB, Peterson MD: Hemodynamic and cardiovascular effects of isoflurane and halothane anesthesia in children. Anesthesiology 66:328, 1986

Department of Anesthesiology
Yale University School of Medicine
333 Cedar Street
New Haven, CT 06510

0889–8537/88 $0.00 + .20

Doppler Echocardiography

*Kenneth R. LaMantia, MD**

Velocity measurements by devices using the Doppler principle have recently increased in importance in anesthesiology and critical care. Increased interest in noninvasive physiologic monitors has promoted the development of sophisticated devices to assess blood flow velocity. Advances in electronic instrumentation have allowed the production of smaller transducers capable of placement into previously inaccessible locations. This article focuses on the use of the Doppler principle to measure blood flow in the heart and great vessels and the importance of such measurements in diagnosing disease, monitoring physiologic function, and guiding therapy with emphasis on disease states commonly encountered by the anesthesiologist.

PHYSICAL PRINCIPLES OF DOPPLER MEASUREMENTS

The Doppler Principle

The first scientific description of the dependence of sound pitch on the relative motion between observer and sound source is credited to Christian Doppler in 1842.[18] The Doppler principle states that the frequency of sound, produced or reflected by a moving object, is altered depending on whether the object is moving toward (higher frequency) or away (lower frequency) from the observer. The shift in sound frequency noted by the observer, known as the Doppler shift, can be used to calculate the relative velocity between the sound emitter and observer.

The relationship between the speed, wavelength, and frequency of sound is given by the following equation:

$$c = fx \tag{1}$$

where c = speed of sound ($1560 \text{ M} \cdot \text{sec}^{-1}$ in biologic tissue), x = wavelength, and f = frequency. The speed of sound is constant in biologic tissue, while frequency and therefore wavelength are changed according to the Doppler principle. The frequency of audible sound is 20 to 20,000 Hz, while diagnostic ultrasound is generally in the 1 to 10 MHz range and is therefore not audible.

---

*Assistant Professor, Department of Anesthesiology, Yale University School of Medicine; Chief, Anesthesiology Service, West Haven Veterans Administration Medical Center, New Haven, Connecticut

With diagnostic ultrasound, it is assumed that sound is emitted from a stationary transducer and subsequently reflected from a moving object relative to the point of origin at the transducer. The mathematical description of this special case is given by the following equation:

$$\mathrm{fd} = \frac{2\ \mathrm{fo}\ \mathrm{V} \cos\theta}{\mathrm{c}} \tag{2}$$

where fd = Doppler shift frequency, c = speed of sound, fo = emitted sound frequency, V = velocity of the object reflecting the emitted sound back to the transducer, and cos θ = angle between the transducer and the direction of blood flow. Rearranging these terms to solve for the velocity of the moving object yields:

$$\mathrm{v} = \frac{\mathrm{fd} \times \mathrm{c}}{2\ \mathrm{F} \times \cos\theta} \tag{3}$$

Velocity measurements and the cross-sectional area (A) through which blood is flowing may be combined to calculate volumetric flow (Fv):

$$\mathrm{Fv} = \mathrm{V} \times \mathrm{A} \tag{4}$$

In the case of blood velocity measurement, the velocity is that of the red blood cells reflecting the sound back to the transducer. If the sound beam is parallel to the direction of blood flow, then the $\cos\theta = 1$ and the maximum velocity of flow in the vessel is measured. Since it is clinically impractical at times to image parallel to the axis of the vessel, velocity may require correction by the cos θ (Fig. 1).

DOPPLER MEASUREMENT OF BLOOD VELOCITY

The application of the Doppler principle to the measurement of blood flow velocity requires a source of sound waves of known frequency, red blood cells in motion in a vessel or heart chamber, and a receiver capable of measuring the Doppler shift. Examination of each of these components will enable the development of a greater understanding of the potential and pitfalls of Doppler flow measurements.

Physics of Blood Flow

Blood is a complex tissue composed of cellular and noncellular components. In blood vessels with a radius greater than 1 mm, blood generally has a parabolic velocity profile (Fig. 2A). Flow velocity at the apex of the profile is higher than at the edges where blood "drags" along the vessel wall. As blood velocity increases, flow eventually

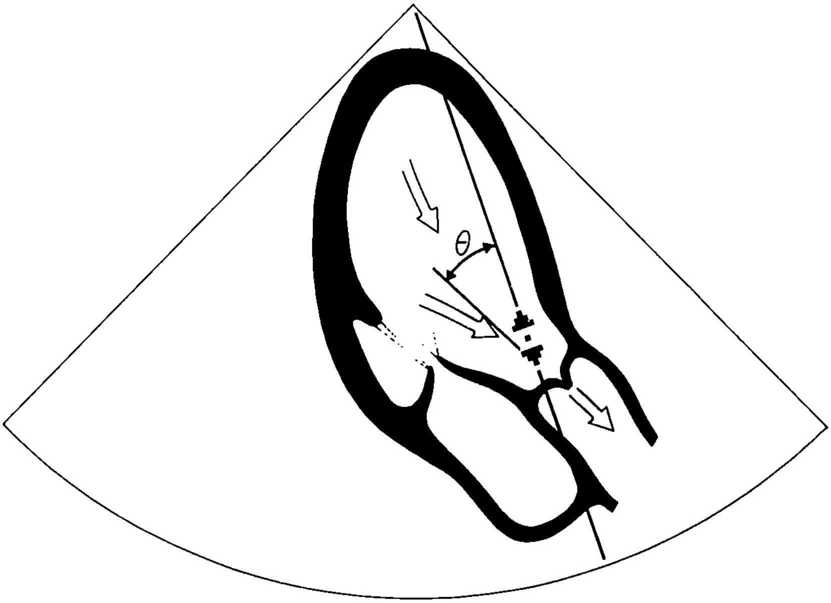


Figure 1. The measurement of blood flow velocity by Doppler ultrasound. The measured velocity must be corrected for the angle (cos θ) between the axis of blood flow. (Reproduced with permission from Hewlett Packard.)

becomes turbulent. The flow profile is no longer parabolic, but characterized by "eddy" formation with the velocity changing rapidly with respect to direction and magnitude. Transition to a turbulent pattern is most likely to occur in pathologic conditions such as vascular or cardiac valvular stenosis (Fig. 2*B*). The detection of a turbulent flow pattern can therefore have great diagnostic significance.

Doppler Techniques

Doppler instrumentation must be capable of directing a sound beam to the moving column of blood and the specific target of interest. The production of the Doppler signal will be considered in three stages: (1) production of the interrogating sound beam, (2) scattering of the sound by the moving object, and (3) display of the velocity measurement.

The production of the Doppler acoustic beam begins at the transducer where an electrical potential is applied to piezoelectric ceramic resulting in a change in its dimension.[25] During this process, sound is emitted and transmitted as a beam through an acoustically coupled medium. In Doppler flow imaging, moving red blood cells act as the backscattering target. Reflected sound returns to the piezoelectric crystal where it is transduced to an electrical signal. Subsequent processing of the signal can be used to produce an auditory and visual display of the Doppler frequency shift. The two basic modes of Doppler examination are: *continuous wave* and *pulsed wave*. Each tech-

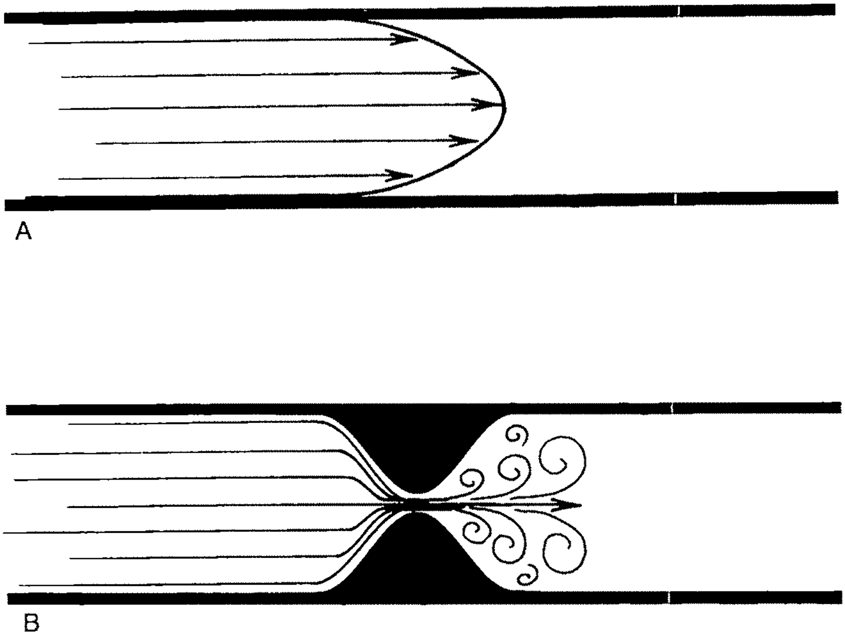


Figure 2. (*A*) Laminar flow velocity of blood in a vessel. Velocity is greater at the center of the vessel than at the fluid vessel wall interface. (*B*) Turbulent flow characteristic of blood acceleration through a stenoic lesion. Blood flow distal to the stenosis varies greatly with respect to flow direction and magnitude in adjacent areas of the vessel. (Reproduced with permission from Hewlett Packard.)

nique has its advantages and limitations providing complementary information about flow.

Continuous Wave Doppler

The technique of continuous wave Doppler (CW) is illustrated in Figure 3. The CW transducer is divided into two isolated crystals; one transmitting continuously and the other receiving continuously. The frequency of transmitted and returning sound differs by the Doppler frequency shift. Sound may be reflected back to the receiving crystal from anywhere along the beam path but a Doppler shift will occur

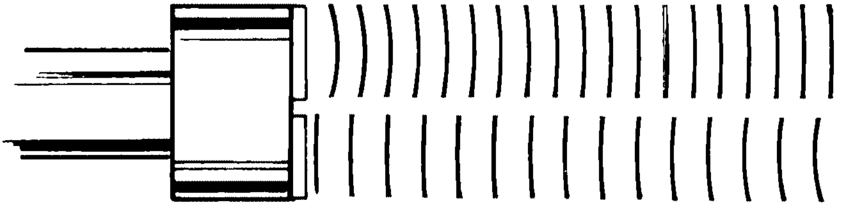


Figure 3. Continuous wave Doppler probe illustrating continuous transmission and reception of sound waves. The surface of the probe is divided into two piezoelectric crystals that function continuously as transmitter and receiver. (Reproduced with permission from Hewlett Packard.)

only if blood is moving relative to the transducer. If the Doppler beam is parallel to blood flow, the angle between them will be zero ($\cos \theta = 1$) and the maximum possible Doppler shift will be measured. A beam perpendicular to the same flow pattern ($\cos 90° = 0$) will result in no Doppler shift and therefore no detectable flow. Dividing the detected shift by the cosine of the angle between the beam and the direction of blood flow is frequently referred to as *angle correction*. For clinical measurements, angle correction of 20° or less is usually ignored as it results in an error of approximately 5 per cent. CW Doppler provides information only about the velocity of flow and its relative direction. Further, any moving object capable of producing acoustic backscatter may be detected (for example, heart valves). As CW does not allow the user to spatially locate the detected flow patterns, the detected Doppler signals may emanate from any location along the transmitted sound beam. Therefore, this technique lacks so-called *range resolution* or the ability to localize the flow signal. To obtain this type of information, pulsed wave Doppler must be employed.

Pulsed Wave Doppler

Pulsed wave (PW) Doppler technique is based on intermittent sound transmission (Figs. 4*A* and *B*). Emitted bursts of sound are transmitted periodically at a frequency known as the *pulse repetition frequency* (PRF). This is defined as the number of sound pulses emitted per second. The intermittent nature of PW sound transmission is the critical difference from the CW technique. PW Doppler uses a single crystal transducer that functions as both transmitter and receiver in order to determine the precise location along the sound beam that blood flow velocity is sampled. The PW transducer emits sound of known frequency for a finite period and then awaits its return. The period between pulses is specified by the time it takes a sound wave to make the round trip between the transducer and the point of interest under examination. As sound travels at constant velocity, the depth of the tissue target, known as the *range gate* specifies the waiting period between pulses. This time period divided into 1 second gives the pulse repetition frequency (PRF). PRF is important because it defines the maximum detectable Doppler frequency detectable ($fd = 1/2$ PRF).[19] This is known as the Nyquist equation and half PRF is the *Nyquist limit*. As the Doppler shift is proportional to blood velocity, this places an upper limit on the maximum velocity measurable by the PW technique. When PW is used to assess velocities beyond the Nyquist limit, a phenomenon known as *aliasing* results, preventing quantitative measurements. The actual upper limit of maximum velocity measurements by PW is based on a number of factors, including the PRF, depth of the target tissue sampled, and transducer frequency (Fig. 5). In order to know the range of the returning signal only one impulse can be in transit between the transducer and the target. The deeper the target, the longer the transit time necessitating a lower PRF. Unfortunately, lower PRFs decrease the

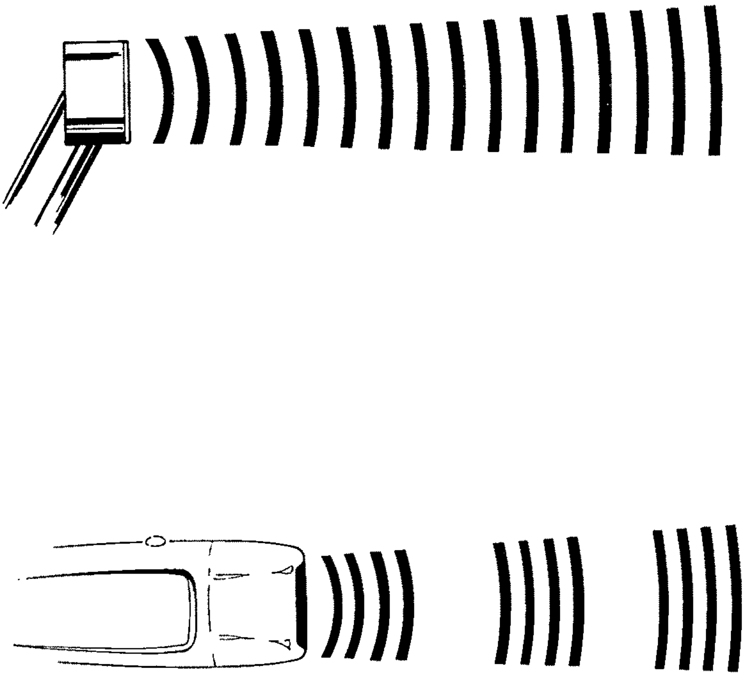


Figure 4. Comparison of continuous wave Doppler emission (*A*) and pulsed Doppler ultrasound (*B*). While continuous wave ultrasound emits sound continuously, the pulsed Doppler transducer emits intermittant sounds or pulses. The frequency of emission is known as the pulse repetition frequency. (Reproduced with permission from Hewlett Packard.)

maximal measurable velocities. A comparison of CW and PW Doppler modalities helps to place the utility of each in perspective (Table 1).

Display of Doppler Flow Data

Doppler flow signals are evaluated by both auditory output and visual display. Each represents Doppler shift of sound frequency that is proportional to the velocity of the blood flow under measurement. The change in emitted sound frequency is equal to 1.3 kHz per 1 mHz transducer frequency, per meter, per second of flow velocity.[19] Simple calculation reveals that maximal velocities encountered in clinical medicine create shifts in the audible range for transducers with a frequency of 3.5 mHz of below. The audible signal output available on most Doppler systems is a semiquantitative measurement of blood flow velocities. Auditory output assists the examiner in conducting a thorough search for maximal velocity signals. A harsh tone indicates the broad spectrum of frequencies associated with turbulent flow. For quantitative analysis, and to facilitate communication, visual display of the frequency spectrum is essential. While a number of methods are

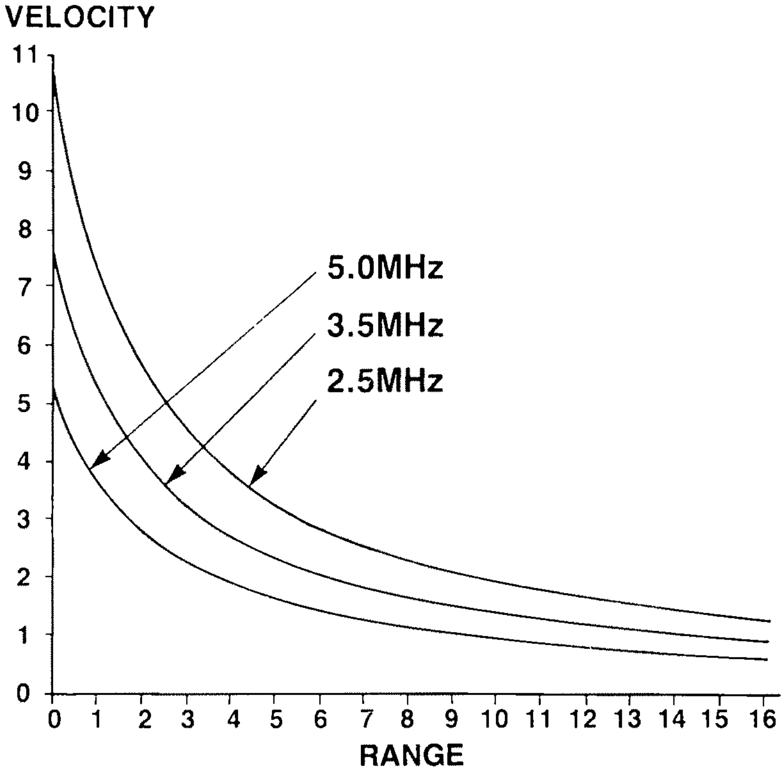


Figure 5. The relationship between target depth (range), transducer frequency, and maximal measurable velocities by pulsed wave Doppler. At any depth, the lower the frequency, the higher the measurable velocity. Targets closer to the transducer allow higher velocity measurements as the transit times are shorter allowing a higher pulse repetition frequency. Velocity, meters per second; range cm. (Courtesy of Hewlett Packard.)

available to solve for the frequencies (that is, velocity) contained in the Doppler signal, the fast Fourier transform has found extensive use in modern echocardiographic systems.[12] This technique is able to solve for the separate frequency components of the Doppler signal and then display the information as a velocity-time plot. The information is presented real-time on a video display and can be captured on a video cassette recorder of other "hardcopy" device.

Table 1. *Comparison of Continuous and Pulsed Wave Doppler*

PROPERTY	PULSED WAVE	CONTINUOUS WAVE
Quantitatively measure high velocities	No	Yes
Aliasing at high velocity	Yes	No
Spatially localizes flow range gating	Yes	No
Simultaneous Doppler and imaging possible	Yes	No

Color Flow Mapping

Color flow mapping (CFM) is a subset of PW Doppler with all the advantages and disadvantages of that modality.[44] It conveys information about the direction and velocity of blood movement in the imaged structure. This information is presented by color encoding of velocity measurements displayed on a two-dimensional or M-mode echogram. As PW Doppler information must be gathered and displayed over the entire sector very rapidly, this process is completely automated. While the ultrasonographer chooses where to place the sample volume in standard PW Doppler, in CFM the entire sector is scanned sequentially for blood flow.

The time requirements for acquiring and displaying the velocities for an entire sector necessitates the application of a new signal processing technique to the Doppler signal. CW and PW modalities rely primarily on the fast Fourier transform to process the Doppler signal and display the velocity spectrum for analysis. These calculations are too time consuming to solve real-time and produce a color flow map. Instead, a technique known as *autocorrelation* is used.[35] This analysis compares the transmitted and returned sound wave for phase differences, assigning a mean velocity to the sample volume. The autocorrelator assigns velocities from a multiple sample sites with a delay of only 1 to 2 ms. This technique allows for the construction of a flow map over the entire echogram sector.

Color is the medium for expressing the velocity estimates on the flow map. While color schemes vary, current usage favors assigning red (warm colors) to motion toward the transducer and blue (cool colors) to motion away from the transducer. The scheme chosen is usually indicated as a color bar on the video display and may be user selectable. The magnitude of the velocity measurement is designated by assigning it a specific hue or brightness of color. The brighter the color the higher the velocity. As with all PW Doppler systems, aliasing occurs when the blood velocities exceed approximately half the sampling rate. Aliasing is displayed as color reversal. That is, red becomes blue and blue becomes red. By noticing the location of adjacent colors on a map, one can usually detect aliasing and not confuse it with blood flow in the opposite direction. Another type of information gained by examining a CFM is the presence of turbulence.[44]

The distinguishing characteristic of turbulence is rapidly changing blood velocities (magnitude and direction) over a small area of the imaged structure. The autocorrelator is able to detect turbulence and designates it with a distinct color, frequently a shade of green. This creates areas of turquoise or yellow, depending on the predominant flow direction. A mosaic pattern is the end result in highly turbulent regions. Such turbulence patterns may provide valuable evidence of blood flowing through stenotic valves or blood vessels.

The ultimate role of CFM in Doppler imaging remains to be defined.[10,44] Applications are likely in the study of stenotic valvular lesions,[45] valvular regurgitation,[52] and congenital heart disease.[51] Several areas of application are described in the sections on specific lesions.

DOPPLER MEASUREMENTS OF CARDIAC OUTPUT

Cardiac output is generally measured by invasive methods using either the Fick method or an indicator dilution technique. As invasive measurements are hazardous and not always clinically indicated, a reliable noninvasive method of measurement is highly desirable. Numerous investigators have applied Doppler technology to cardiac output measurements.[4,6,7,13,22,41] A review of Doppler methods of cardiac output determination has been recently published.[3]

Basic Considerations

Cardiac output is expressed as volume flow per unit time. In the clinical setting this is generally expressed in units of liters per minute indexed for body surface area (cardiac index). Doppler ultrasound measures blood flow in units of velocity such as meters per second or centimeters per second. The entire process of cardiac output measurement by Doppler may be conceptualized as constructing a cylinder of a volume equal to the stroke volume. The length of the cylinder is equal to the area under the maximal flow velocity curve determined by planimetry. The cross-sectional area of the cylinder is equal to the area of the anatomic structure where flow velocity is measured. The measurement site chosen in generally a heart valve or great vessel. The product of cylinder length and area is equal to the stroke volume (Fig. 6). Cardiac output is then computed by multiplying the stroke volume by heart rate.

Sites for Measuring Cardiac Output

Measurement of cardiac output by the Doppler technique (CO_D) has been made at a number of sites within the heart and great vessels, including the ascending aorta.[3,4,6,7,15,22,24,26,36,41,43] Two types of data are required to make determinations of volumetric flow: (1) flow velocity, and (2) aortic dimension (see equations 3 and 4).

Flow velocity measurements are obtained by CW or PW Doppler. For PW, the sampling volume is placed in the ascending aorta, generally at the level of the sinotubular junction[24] or aortic annulus.[26] The spectral display time-velocity integral is measured for 3 to 10 beats, and the results are averaged. Measurement of the cross-sectional area is based on two-dimensional echocardiography[26] or M-mode images of the aorta in the parasternal two-chamber long axis from the chest wall. The aorta may be measured at the valve ring, valve leaflets, or beyond the sinuses of valsalva.[16] Comparison of

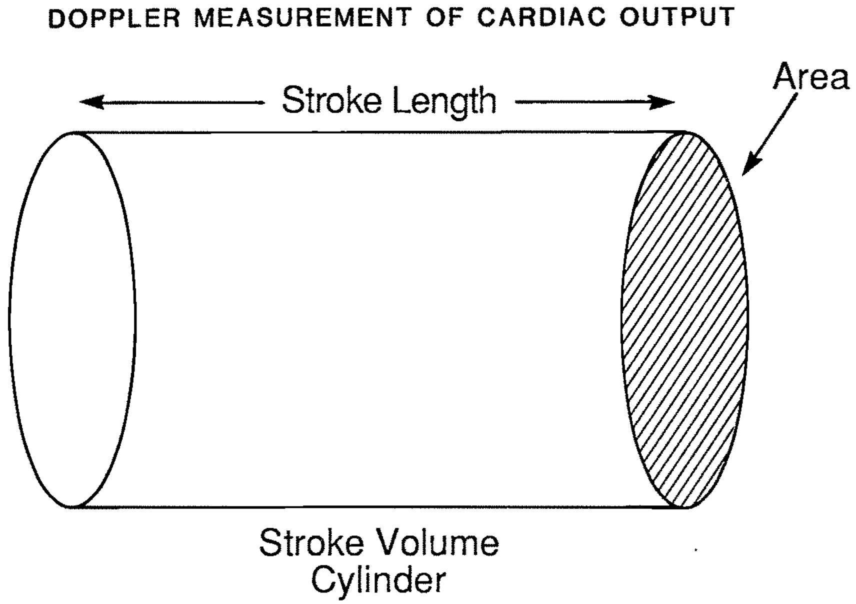


Figure 6. Determination of CO by Doppler techniques. Step 1, determine cross-sectional area of the stroke volume cylinder, which is the valve area or vessel cross-sectional area of the site of velocity measurement. Step 2, measure flow velocity integral at this location using Doppler ultrasound and derive stroke length. Step 3, multiply the heart rate by the product of cross-sectional area (step 1) and the flow velocity integral (step 2) to solve for volumetric flow (cardiac output).

Doppler cardiac output (CO_D) and thermodilution cardiac output (CO_{TD}) measurements have been encouraging ($r = 0.95$).[4]

The other major site used for CO_D measurements is the mitral valve.[13,26,31,32] Mitral techniques use a variable number of views to obtain the necessary diameter and velocity measurements. One method employs short- and long-axis (four-chamber) views of the valve obtained from parasternal and apical transducer locations on the chest wall.[13] Both two-dimensional and M-mode imaging of the mitral valve is used to calculate the cross-sectional area of flow through the orifice. In one series of experiments this method was validated in an open chest canine model where cardiac output was controlled with a roller pump right heart bypass preparation. Regression analysis of correlations of CO_D and roller pump controlled cardiac output revealed $r = 0.974$.[13] In adult patients this technique is more difficult in practice because the several views required are not always easily obtained.[43] For this reason, a simplified technique to measure CO_D at the mitral valve has been developed.[31] This method employs only a long-axis view of the mitral valve (five-chamber view) from the cardiac apex, which is simple to obtain.

Dedicated Doppler Cardiac Output Monitors

A recent approach to Doppler measurement of cardiac output has been the dedicated cardiac output monitor.[14,30,39] Such devices including the Accucom (Datascope Corp., Paramus, NJ), employ CW Doppler without imaging ultrasound to determine cardiac output. Such devices use suprasternal CW Doppler measurement of maximal velocity in the ascending aorta combined with a nomogram to predict aortic diameter to calculate cardiac output. The user can specify an aortic diameter rather than depend on the nomogram for the cross-sectional area calculation. The final step in continuously monitoring cardiac output is the placement of the esophageal CW transducer mounted within an esophageal stethoscope. The suprasternal cardiac output measurement is used to calibrate the esophageal measurement because descending aortic flow does not represent total cardiac output (the head and neck are not included). The esophageal probe continuously updates the cardiac output determination, which is digitally displayed.

Several studies have reported on the reliability of esophageal cardiac output monitoring. When comparing Doppler cardiac output by Ultracom (Lawrence Medical Systems) with thermodilution cardiac output, investigators found a poor correlation. However, after correcting for calibration errors the correlation coefficient was improved, $r = 0.92$.[30] This same study found excellent tracking of cardiac output with the esophageal Doppler. The ability to track cardiac output with the dedicated cardiac output monitor decreased after cardiopulmonary bypass in patients undergoing open heart surgery.[30] Because noninvasive measurements of cardiac output are likely to find applicability during surgical procedures other than open heart procedures where invasive measurements are generally available, this finding does not detract from its use. The future of esophageal cardiac output monitoring will depend on further investigation of its utility in patient management in the absence of pressure correlates of ventricular filling.

DOPPLER EVALUATION OF VALVULAR FUNCTION

Doppler echocardiography has added to the clinician's ability to diagnose and treat patients with valvular heart disease. Doppler can be used not only to diagnose valvular stenosis and regurgitation, but to quantitate its severity. This technology is finding increased use in the operating room to monitor patients with valvular disease as well as to guide surgical repair of valve dysfunction.

Doppler Evaluation of Valvular Stenosis

One of the most important clinical uses of Doppler echocardiography has been in the diagnosis and quantitation of stenotic lesions.[48] Before describing the changes seen in Doppler signals secondary to valvular stenosis, the physical basis for quantitating stenotic lesions is described.

Flow through heart valves is generally laminar with maximum velocities of less that 2 meters per sec, which are easily measured by PW Doppler. When blood flows through a stenotic lesion, acceleration occurs creating turbulent flow and jet formation. Flow velocities increase and can no longer be accurately measured by PW Doppler as the Nyquist limit is exceeded. For this reason, CW Doppler is employed for quantitation of maximal flow velocity. When stenosis occurs there is a pressure drop across the lesion that behaves like an orifice and can therefore be described by the Bernoulli equation.[11] This states that the pressure gradient across an orifice is determined by three components: (1) convective acceleration, (2) flow acceleration, and (3) viscous friction:

$$\underset{\substack{\text{pressure}\\ \text{gradient}}}{P_1 - P_2} = \underset{\substack{\text{convective}\\ \text{acceleration}}}{1/2\rho(V_2^2 - V_1^2)} + \underset{\substack{\text{flow}\\ \text{acceleration}}}{\rho \int_1^2 dv/dt\, ds} + \underset{\substack{\text{viscous}\\ \text{friction}}}{R(v)} \qquad (5)$$

where P_1, P_2 = pressures on either side of the orifice, $V_1 - V_2$ = velocity on either side of the orifice, ρ = density of blood, ds = distance over which the pressure is measured, R(v) = viscous resistance of the vessel, dv = change in velocity during valve opening, and d(t) = time for valve opening. This equation can be simplified under clinical conditions because flow acceleration and viscous friction can be neglected if gradients are measured at peak velocity. As $1/2\ \rho = 4$, the equation becomes

$$P_1 - P_2 = 4(V_2^2 - V_1^2)$$

If the blood flow velocity proximal to the stenosis is less than 1 m per second, V_1 can be ignored, further simplifying the equation:

$$P_1 - P_2 = 4V^2$$

Thus, the gradient can be estimated from measurement of the maximal jet velocity distal to the obstruction by CW Doppler.

Doppler evaluation of valvular function is an adjunct to a full echocardiographic examination. Two-dimensional and M-mode imaging usually reveal that stenosis is present but does not accurately determine its significance hemodynamically, particularly in the elderly.[9] PW is useful to localize the area of stenosis and to evaluate concomitant valvular regurgitation. CW enables the ultrasonograher to quantitate the gradient by application of the simplified Bernoulli equation.

Aortic Stenosis

Several studies have documented the utility of CW Doppler measurements of aortic stenosis gradients in children[21,27] and adults.[8] In elderly patients with calcific aortic stenosis, correlation with simultaneous catheterization derived gradients are good ($r = 0.92$). These techniques are difficult to compare because Doppler measures instantaneous gradients while the catheterization measurement is peak to peak, which is smaller. The two measurements approach each other as stenosis becomes more severe.

As pressure gradients in aortic stenosis are dependent not only on valve area, but also on cardiac output, stenosis can be underestimated if CO is depressed. For this reason methods to estimate valve area have been investigated and evaluated using the so-called *continuity equation.*[46] This equation states that the products of velocity and cross-sectional area on either side of a stenotic lesion are equal. Doppler estimates of aortic valve area when compared to catheterization data yield clinically useful correlation coefficients ($r = 0.89$).[46]

Mitral Stenosis

PW Doppler is virtually 100 per cent sensitive and specific in detecting mitral stenosis.[47] As velocity measurements generally exceed 1.5 m per second, aliasing may occur on PW examination necessitating use of CW for quantification. Obstruction results in a decreasing slope of the early filling wave (E wave) measured just beyond the mitral valve orifice in the left ventricle. The time required for this early wave to decrease to 50 per cent of the maximum pressure has been called the pressure half time ($P_{t1/2}$). Normal mitral valve $P_{t1/2}$ is less than 60 msec. With $P_{t1/2}$ exceeding 220 msec the mitral valve area is generally less than 1 cm^2 (normal = 4 to 6 cm^2).[47] A study comparing $P_{t1/2}$ by Doppler with angiographic calculations of valve area revealed good correlations ($r = 0.85$).[37]

Doppler Measurement of Regurgitant Lesions

The Doppler examination for valvular regurgitation is highly sensitive and specific. Lesions that are missed frequently are of nonrheumatic origin with eccentric jets. In these cases, color flow mapping may make detection of such jets more reliable.

Mitral Regurgitation. Mitral regurgitation is detected by Doppler echocardiography in virtually all patients with angiographically significant lesions.[47] The velocity of regurgitant jets usually exceeds the maximal limits of PW measurements. For this reason the CW Doppler is necessary to measure maximal velocities. Several techniques have been used to quantitate mitral regurgitation. The most common method is mapping the jet within the left atrium.[2,40,54] Several conditions may cause underestimation of mitral regurgitation severity including a large atrium[2] and low cardiac output. Eccentric jets from prosthetic values may also result in underestimation of mitral regurgitation.

Color flow mapping provides a sensitivity of 94 per cent and specificity of 100 per cent for detecting mitral regurgitation.[42] Color flow mapping has advantages over PW or CW doppler in detecting small eccentric jets. The severity of mitral regurgitation has generally been graded by the depth to which the jet extends into the left atrium. A wide jet with aliasing of colors and a mosaic pattern indicates significant mitral regurgitation. The area of the planimeterized jet compared with the area of the left atrium correlates with the angiographic grading system.[42] Quantitative approaches to assessment of mitral regurgitation by CFM are still under development.

Aortic Regurgitation. Doppler echocardiography provides valuable information about the presence and severity of aortic regurgitation.[1,17,53] While M-mode and two-dimensional echocardiography provide indirect evidence of aortic regurgitation, such as diastolic fluttering of the mitral and aortic valves, Doppler studies are usually diagnostic.

Doppler quantitation of aortic regurgitation falls into two general categories of methods similar of those used to evaluate mitral regurgitation: (1) jet mapping techniques, and (2) flow measurements distal to the aortic valve. In this lesion, mapping techniques have not proved to be highly reliable. Measurements of reverse and forward flow in the ascending aorta distal to the jet and in the aortic arch have provided reasonable estimates of regurgitant fraction when combined with measurements of aortic diameter.[5] One study reported an excellent correlation ($r = 0.90$) between Doppler estimates of regurgitation and invasive measurements.[53]

Color flow mapping has added an additional modality to quantitate aortic regurgitation.[52] Early attempts at quantitation centered on measurement of the jet length in the left ventricular cavity.[38] Jets extending to the ventricular apex were considered severe. Subsequent work appears to indicate that the width of the jet at the level of the left ventricular outflow tract may be a better indicator of severity of aortic regurgitation independent of afterload.[5] The ultimate role of quantitative color flow mapping in quantitation of aortic regurgitation remains unclear.

Congenital Heart Disease

Doppler ultrasound plays an important role in the diagnosis and treatment of congential heart disease. The anatomic and pathophysiologic complexity of congenital heart disease provides an important area of application for all types of Doppler velocity measurements. More comprehensive treatment of Doppler in congenital heart disease is available elsewhere.[33,49]

Cardiac output can be measured in a variety of sites in pediatric patients by Doppler techniques. Measurements in the ascending aorta, pulmonary artery, and tricuspid valve have been employed successfully.[28]

Shunt calculations and the ratio of pulmonary to systemic flow (Qp/Qs) can be derived based on the techniques developed for cardiac output measurements. Determination of pulmonary artery and aortic flows are based on diameter and flow velocity measurements using M-mode or two-dimensional echocardiography and Doppler. The ratio of flows gives the Qp/Qs ratio. Coarctation of the aorta is diagnosed by detecting a high velocity jet in the descending aorta.[20] Application of the Bernoulli equation yields the calculated pressure gradient across the stenosis.

Atrial Septal Defects. Doppler echocardiography is an extremely sensitive method of detecting atrial septal defects (ASD).[20,34,49] Doppler examination reveals left-to-right flow through the defect beginning in midsystole and extending to early diastole. A second period of flow into the right atrium occurs with atrial contraction. In early systole a brief right-to-left flow occurs in many patients with simple atrial septal defect. Doppler evidence of an atrial septal defect is easily demonstrated when two-dimensional echocardiography fails to demonstrate the site of defect.[23] Color flow mapping is especially useful in determining the presence of multiple atrial septal defects and ostium primum defects.[51]

Ventricular Septal Defects. Ventricular septal defects in children with normal right ventricular pressures reveal left-to-right shunting by CW and PW Doppler.[29,50] In the PW examination, the sample volume is placed in the right ventricle to detect the flow pattern. Flow is usually demonstrated throughout systole in small to moderate defects. Large shunts with high right ventricular pressures may not reveal high flows as pressures have equalized between left and right ventricles. Diastolic flow may be seen with small defects with accentuation during atrial contraction.[33] Color flow mapping appears to be useful in demonstrating multiple ventricular septal defects especially of the muscular type.[51] This may obviate the need for cardiac catheterization. A perioperative use of color flow mapping is the detection of postrepair defects. Such defects can be demonstrated in the operating room with application of epicardial imaging.

FUTURE DIRECTIONS

The applications for Doppler echocardiography within the perioperative setting are virtually inexhaustible. Doppler cardiac ultrasound provides the anesthesiologist with a window on cardiac function that is unrivaled by invasive techniques including pulmonary artery catheterization. Combined imaging and Doppler echocardiography enables the anesthesiologist to gain a deeper appreciation of hemodynamics than has been previously possible in the operating room. Several areas of development would increase the applicability of Doppler for intraoperative monitoring and diagnosis.

The incorporation of continuous wave Doppler into the transesophageal echoscope would allow quantitative measurements in pathologic conditions where aliasing prevents PW flow velocity determination. Alternate approaches would include multigated pulsed wave Doppler techniques. Minaturization of the transesophageal echocardiography probe would allow for applications in the pediatric population where noninvasive monitoring plays a paramount role in clinical care.

Color flow mapping is currently a qualitative or semiquantitative technique at best. Further work on its applicability to quantitate lesions producing flow abnormalities is essential. Three-dimensional display of echocardiography images may ultimately reduce the need for invasive angiography. Finally, more convenient methods to store images real-time and quantitate flow automatically by computer-driven graphic analysis software would reduce user interaction in producing quantitative data such as cardiac output measurements. This would greatly increase the clinical utility of Doppler technology in the perioperative environment. Multidisciplinary approaches will be essential in reaping the obvious benefits of the Doppler evaluation of blood flow velocity.

REFERENCES

1. Abbasi AS: The role of Doppler echocardiography in valvular insufficiency. *In* Berger M (ed): Doppler Echocardiography in Heart Disease. New York, Marcel Dekker, 1987
2. Abassi AS, Allen MW, DeCristofaro D, et al: Detection and estimation of the degree of mitral regurgitation by range gated Doppler echocardiography. Circulation 61:143, 1980
3. Ascah KJ, Stewart WJ, Levine RA, et al: Doppler-echocardiographic assessment of cardiac output. Radiol Clin North Am 23:659, 1985
4. Boucheard A, Blumlein S, Schiller NB, et al : Measurement of left ventricular stroke volume using continuous wave Doppler echocardiography of the ascending aorta and M-mode echocardiography of the aortic valve. J Am Coll Cardiol 9:75, 1987
5. Byard CE, Perry GJ, Roitman DI, et al: Quantitative assessment of aortic regurgitation by color Doppler. Circulation 72:111–146, 1985
6. Chandraratna PA, Nanna M, McKay C, et al: Determination of cardiac output by transcutaneous continuous-wave ultrasonic Doppler computer. Am J Cardiol 53:234, 1984
7. Colocousis JS, Huntsman LL, Curreri PW: Estimation of stroke volume changes by ultrasonic Doppler. Circulation 56:914, 1977
8. Currie PJ, Seward JB, Reeder GS, et al: Continuous-wave Doppler echocardiographic assessment of severity of calcific aortic stenosis: A simultaneous Doppler-catheter correlative study in 100 adult patients. Circulation 71:1162, 1985
9. DeMaria AN, Brommer W, Joye J, et al: Value and limitations of cross-sectional echocardiography of the aortic valve in diagnosis and quantification of valvular stenosis. Circulation 62:304–312, 1980
10. DeMaria AN, Smith MD, Kwan OL: Doppler flow imaging: Another step in the evolution of cardiac ultrasound. Echocardiography 2:495–500, 1985
11. Epstein BS, Berger M: Physical principles of Doppler ultrasound, Doppler instrumentation, and blood flow dynamics. *In* Berger M (ed): Doppler Echocardiography in Heart Disease. New York, Marcel Dekker, 1987, pp 1–46
12, Feigenbaum H (ed): Instrumentation in Echocardiography. Philadelphia, Lea & Febiger, 1986, pp 1–49
13. Fisher DC, Sahn DJ, Friedman MJ, et al: The mitral valve orifice method for noninvasive two-dimensional echo Doppler determinations of cardiac output. Circulation 67:872, 1983
14. Freund PR, Padavich CA: A comparison of cardiac output techniques: Transesophageal versus thermodilution cardiac output during general anesthesia in man [abstract]. Anesthesiology, September 1985
15. Gardin JM, Dabestani A, Matin K, et al: Reproducibility of Doppler aortic blood flow measurements: Studies on intraobserver, interobserver and day-to-day variability in normal subjects. Am J Cardiol 54:1092, 1984
16. Gardin JM, Tobis JM, Dabestani A, et al: Superiority of two-dimensional measure-

ment of aortic vessel diameter in Doppler echocardiographic estimates of left ventricular stroke volume. J Am Coll Cardiol 6:66, 1985
17. Goldberg SJ, Allen HD: Quantitative assessment by Doppler echocardiography of pulmonary or aortic regurgitation. Am J Cardiol 56:131, 1985
18. Hatle L, Angelsen B: Doppler Ultrasound in Cardiology: Physical Principles and Clinical Applications (ed 2). Philadelphia, Lea & Febiger, 1985
19. Harrigan P, Lee R: Technology of Doppler echocardiography: Capabilities and limitations. *In* Principles of Interpretation in Echocardiography. New York, John Wiley and Sons, 1985
20. Hatle L, Angelson B: Pulsed and continuous wave Doppler in diagnosis and assessment of various heart lesions. *In* Doppler Ultrasound in Cardiology. Philadelphia, Lea & Febiger, 1985, pp 97–282
21. Hatle L: Noninvasive assessment and differentiation of left ventricular outflow obstruction with Doppler ultrasound. Circulation 64:381, 1981
22. Huntsman LL, Stewart DK, Barnes SR, et al: Noninvasive Doppler determination of cardiac output in man. Circulation 67:593, 1983
23. Kalmanson D, Veyart C, Derai C, et al: Noninvasive technique for diagnosing atrial septal defect and assessing shunt volume using directional Doppler ultrasound. Br Heart J 34:981–991, 1972
24. Labovitz AJ, Buckingham TA, Habermehl K, et al: The effects of sampling site on the two-dimensional echo-Doppler determination of cardiac output. Am Heart J 109:327, 1985
25. Levine RA, Gillam LD, Weyman AE: Echocardiography in cardiac research. *In* Fozzard HA, Haber E (eds): The Heart and Cardiovascular System: Scientific Foundations. New York, Raven Press, 1986, pp 369–452
26. Lewis JF, Lawrence CK, Nelson JG: Pulsed Doppler echocardiographic determination of stroke volume and cardiac output: Clinical validation of two new methods using the apical window. Circulation 70:425, 1984
27. Lima CO, Sahn DJ, Valdes-Cruz LM, et al: Prediction of the severity of left ventricular outflow tract obstruction by quantitative two-dimensional echocardiographic Doppler studies. Circulation 68:349, 1983
28. Loeber CP, Goldberg SJ, Allen HD: Doppler echocardiographic comparisons of flows distal to the four cardiac values. J Am Coll Cardiol 4:268–272, 1984
29. Magherini A, Azzolina G, Wiechmann V, et al: Pulsed Doppler echocardiography for diagnosis of ventricular septal defects. Br Heart J 43:143–147, 1980
30. Mark JB, Steinbrook RA, Gugino LD, et al: Continuous noninvasive monitoring of cardiac output with esophageal Doppler ultrasound during cardiac surgery. Anesth Analg 65:1013, 1986
31. Meijboom EJ, Horowitz S, Valdes-Cruz LM, et al: A simplified mitral valve method for two-dimensional echo Doppler blood flow calculation: Validation in an open-chest canine model and initial clinical studies. Am Heart J 113:335, 1987
32. Meijboom EJ, Rijsterborgh H, Bot H, et al: Limits of reproducibility of blood flow measurements by Doppler echocardiography. Am J Cardiol 59:133, 1987
33. Meyer RA: Echocardiography. *In* Adams FA, Emmanouilides GC (eds): Heart disease in Infants, Children and Adolescents. Baltimore, Williams and Wilkins, 1983 pp 58–83
34. Mingoe S, Tei C, Kisannki A, et al: Noninvasive pulsed Doppler echocardiographic detection of the direction of shunt flow in patients with atrial septal defect: Usefulness of the right parasternal approach. Circulation 71:745–753, 1985
35. Miyatake K, Okamoto M, Kinoshita N, et al: Clinial applications of a new type of real-time two-dimensional Doppler flow imaging system. Am J Cardiol 54:857–868, 1984
36. Nishimura RA, Callahan MJ, Schaff HV, et al: Noninvasive measurement of cardiac output by continuous-wave Doppler echocardiography: Initital experience and review of the literature. Mayo Clin Proc 59:484, 1984
37. Nishimura RA, Miller FA, Callahan MJ, et al: Doppler echocardiography: Theory, instrumentation, technique and application. Mayo Clin Proc 6:321, 1985
38. Omoto R, Yokote Y, Takamoto S, et al: The developments of real time two dimen-

sional Doppler echocardiography and its clinical significance in acquired valvular disease. Jpn Heart J 25:325, 1984
39. Overand P, LaMantia KR, Barash PB: Transesophageal Doppler ultrasound determination of cardiac output using a nomogram to estimate aortic diameter: Clinical evaluation [abstract]. Int Soc Cardiovasc Anesth, September 1986
40. Quinones MA, Young JB, Wagonner AD, et al: Assessment of pulsed Doppler echocardiography in detection and quantitation of aortic and mitral regurgitation. Br Heart J 42:612, 1980
41. Rose JS, Nanna M, Rahimtoola SH, et al: Accuracy of determination of changes in cardiac output by transcutaneous continuous-wave Doppler computer. Am J Cardiol 54:1099, 1984
42. Saenz CB, Deumite NS, Roitman DI, et al: Limitations of color Doppler in quantitative assessment of mitral regurgitation. Circulation 72(suppl 2):99, 1985
43. Sahn DJ: Determination of cardiac output by echocardiographic Doppler methods: Relative accuracy of various sites for measurement. J Am Coll Cardiol 6:663, 1985
44. Sahn DJ: Real-time two-dimensional echocardiographic flow mapping. Circulation 71:849–853, 1985
45. Skelton TN, Kisslo J: Real-time Doppler color flow mapping in stenotic valvular lesions. Echocardiography 2:523–531, 1985
46. Skjaerpe T, Hegrenaes L, Hatle L: Noninvasive estimation of valve area in patients with aortic stenosis by Doppler ultrasound and two-dimensional echocardiography. Circulation 72:810, 1985
47. Smith MD, Handshoe R, Handshoe S, et al: Comparative accuracy of two-dimensional echocardiography and Doppler pressure half-time methods is assessing severity of mitral stenosis in patients with and without prior commissurotomy. Circulation 73:101, 1986
48. Smith MD, Kwan OL, DeMaria AN: Value and limitations of continuous-wave Doppler echocardiography in estimating severity of valvular stenosis. JAMA 255:3145, 1986
49. Snider AR: Doppler echocardiography in congenital heart disease. *In* Berger M (ed): Doppler Echocardiography in Heart Disease. New York, Marcel Dekker 1987
50. Stevenson JG, Kawayori I, Dooley T, et al: Diagnosis of ventricular septal defect by pulsed Doppler echocardiography: Sensitivity, specificity, and limitations. Circulation 58:322–326, 1978
51. Swensson RE, Sahn DJ, Valdes-Cruz LM: Color flow Doppler mapping in congenital heart disease. Echocardiography 2:545–549, 1985
52. Switzer DF, Nanda NC: Color Doppler evaluation of valvular regurgitation. Echocardiography 2:533–543, 1985
53. Touche T, Prasquier R, Nitenberg A, et al: Assessment and follow-up of patients with aortic regurgitation by an updated Doppler echocardiographic measurement of the regurgitant fraction in the aortic arch. Circulation 72:819, 1985
54. Veyar C, Ameur A, Bas S, et al: Pulsed Doppler echocardiographic indices for assessing mitral regurgitation. Br Heart J 51:130, 1984

Department of Anesthesiology
Yale University School of Medicine
Anesthesiology Service
West Haven Veterans Administration Hospital
333 Cedar Street
New Haven, CT 06510

0889-8537/88 $0.00 + .20

Cardiac Output

*Daniel M. Thys, MD**

The heart, as a pump, generates both pressure and flow. The amount of blood pumped during 1 minute by each ventricle is termed the cardiac output. An average man (70 kg) has a resting cardiac output of 5.5 $L \cdot min^{-1}$, but with heavy exercise it may reach 25 $L \cdot min^{-1}$. Interest in the measurement of cardiac output dates back to William Harvey (1578 to 1657), who first estimated stroke volume by measuring the capacity of the cardiac ventricles. Based on the results of this simple experiment, he concluded that, in a few minutes, the heart had to pump out a greater volume of blood than that contained in the whole body.[41]

Physiologic measurements of cardiac output, however, did not begin before the late nineteenth century. In 1870, Adolph Fick, a German physiologist, first devised an appropriate method for its measurement. Interestingly, Fick's research was primarily in the area of work and heat production in skeletal muscles. The principle, for which he is now famous, came from a diversion in his thoughts and was published as a very brief report.[18] Fick himself never applied his principle to the measurement of cardiac output in vivo.[24]

Today, numerous methods are available for the measurement of cardiac output. They are based on a wide variety of techniques including angiography, scintigraphy, echocardiography, mass spectrometry, and laser Doppler flowmetry. In this article, only methods that are currently applicable in the operating room or are under investigation for such application will be described.

In the discussion of any measurement technique, two important characteristics of the technique should be considered: the *accuracy* and the *precision.*

Accuracy defines the relationship between a measured cardiac output and the actual, or true, cardiac output. The definition implies that the cardiac output, measured by the technique under investigation, is being compared with a measurement obtained by another technique. The other technique should have the attributes of a "gold standard" and should, preferably, be based on a different measure-

---

*Associate Professor of Anesthesiology, Mount Sinai School of Medicine; Director, Division of Cardiothoracic Anesthesiology, Mount Sinai Hospital, New York, New York

ment principle. Results of accuracy tests are often reported as linear regressions. In the evaluation of such results particular attention must be paid to the population in whom the measurements were obtained, the range of the measured values, the relationship between the regression line and the line of identity, and the spread of the data points around the regression line.

Precision defines the reproducibility of a measurement technique. The reproducibility of a method must be known before the results, obtained with the method, can be used for therapeutic decision making. Indeed, the variability, or reproducibility of a technique, determines how many determinations will be required to obtain an accurate measurement. A simple example will clearly illustrate this point. A single cardiac output determination yields a value of 3 $L \cdot min^{-1}$ and based on this result it is decided to administer an inotrope. After the inotrope has been administered, a second cardiac output determination yields a value of 3.5 $L \cdot min^{-1}$. One can then wonder whether the second value reflects a true improvement in cardiac function or the lack of precision of the cardiac output measurement technique.

Whenever possible this article provides information on the accuracy and precision of each of the cardiac output measurement techniques.

THE FICK PRINCIPLE

The measurement of cardiac output, according to the principle first enunciated by Fick, remains of importance today. The Fick principle states that the flow for a given period of time is equal to the amount of a substance entering the stream of flow in the same period of time, divided by the difference between the concentrations of the substance upstream and downstream of the point of entry. In the direct Fick method, the cardiac output is determined from the oxygen consumption and the difference between the arterial and mixed venous oxygen contents. While the direct Fick method is often mentioned as a gold standard for the measurement of cardiac output, it has not been widely used in clinical practice owing to some inherent difficulties related to the measurement of oxygen consumption. However, with the recent introduction of mass spectrometry, interest in the technique has been rekindled and therefore a detailed discussion of this method of cardiac output measurement is worthwhile. In addition, all the indicator dilution techniques, discussed in the next section, are also based on the same principle.

The Measurement and Its Validation

Techniques to measure oxygen consumption and blood oxygen content have long been well established, and therefore oxygen has traditionally been the indicator-substance of choice in the clinical applications of the direct Fick method. The cardiac output is calculated with the following formula:

$$\dot{Q} = \frac{\dot{V}O_2}{(CaO_2 - C\bar{v}O_2) \times 10}$$

where $\dot{Q}$ = cardiac output in $L \cdot min^{-1}$, $\dot{V}O_2$ = oxygen consumption in ml $O_2 \cdot min^{-1}$, CaO_2 = arterial oxygen content in ml O_2 per 100 ml blood, $\bar{v}O_2$ = mixed venous oxygen content in ml O_2 per 100 ml blood, and 10 = factor to convert units to $L \cdot min^{-1}$.

Oxygen consumption is equal to the product of the expired air volume and the difference between the oxygen content in the inspired and expired gas. The expired air volume can be measured by a variety of means, while the difference between the inspired and expired oxygen concentration is determined by gas analysis. For the calculation of the arteriovenous oxygen content difference, arterial and mixed venous blood is sampled. Oxygen consumption and arteriovenous oxygen content differences must be measured in a steady state, because the Fick principle is valid only when tissue oxygen-uptake is equal to lung oxygen-uptake.[33] The accuracy and reproducibility of the direct Fick cardiac output technique have been determined in a variety of animal and human experiments. Several investigators have compared Fick measurements with direct rotameter measurements of cardiac output. The rotameters were inserted into the pulmonary artery and in the venous input circuit to the heart. The rotameter and Fick measurements compared well, within the limits of the accuracy of the rotameters themselves.[32,54,55] A large number of comparisons have been made between the Fick method and the indicator-dilution methods.[8,12,13,15,26,42] While in some of these studies the Fick method yielded slightly lower measurements than the indicator-dilution techniques, in others the reverse was true. The average results showed excellent correlation between the two techniques.

The precision of the direct Fick has also been extensively investigated. In both animals and humans it was found to be excellent, provided steady-state conditions could be achieved.[31,56,65,72]

Limitations

The major limitations of the direct Fick technique are well recognized.[23,24] They are related to errors in sampling and analysis or to the inability to maintain steady-state hemodynamic and respiratory conditions. To minimize errors in sampling, one must ascertain that the venous blood is truly mixed venous blood and that the samples represent average, rather than instantaneous, samples.

The most serious errors in the measurement of cardiac output by the direct Fick technique result from changes in pulmonary volumes. Indeed, the methods used to determine oxygen consumption measure the uptake of oxygen by the lungs rather than by the blood. Since lung volumes can change, the tissues' oxygen consumption is not necessarily being measured.

Recent Developments

With the widespread availability of mass spectrometry, interest in the intraoperative application of the direct Fick principle has again risen. Heneghan et al[29] have designed a system to measure metabolic gas exchange during general anesthesia. It uses a mass spectrometer, a mixing box, and two inert gases. They obtained measurements in patients undergoing cardiac surgery and demonstrated that the variations in inspired and expired minute volumes were within 2 per cent, while they were within 10 per cent for oxygen consumption, carbon dioxide output, and respiratory quotient.[29] These investigators also used this gas measuring system to determine cardiac output during anesthesia, and observed that the cardiac output values obtained with the two inert gases were reproducible but lower than those obtained with the direct Fick principle.[28]

Recently, Davies et al[9] have also attempted to continuously measure cardiac output by means of the Fick principle. To measure oxygen consumption and carbon dioxide production, they used a self-contained instrument (MGM II, Utah Medical Products, Midvale UT) that collects expired gas in a mixing chamber and measures expired ventilation with an ultrasonic flow transducer. Inspired and expired gas samples were alternatively conducted to an infrared CO_2 analyzer and a zirconium oxide O_2 analyzer. In pigs, continuous SaO_2 measurements obtained with a fiberoptic catheter placed in the carotid artery, while continuous $S\bar{v}O_2$ was measured with a second flow-directed pulmonary artery fiberoptic catheter. They compared the continuous Fick with simultaneous thermodilution cardiac outputs, as well as with continuous pulmonary artery electromagnetic flow measurements. Good correlations were obtained between the continuous Fick and the two other methods (Table 1, Fig 1). In humans, SaO_2 was measured by pulse oximetry.[10] The investigators obtained a total of 237 simultaneous Fick and thermodilution cardiac output measurements in 21 ventilated, postcardiac surgery patients. Although the

Table 1. *Comparison of Three Different Methods of Cardiac Output Estimation*

	NO.	r	SEE	SLOPE	INTERCEPT
CFCO versus EMCO (mean ± SD)	1748	0.89 ± 0.06	0.57 ± 0.09	0.99 ± 0.09	0.16 ± 0.39
TDCO versus EMCO (pooled data)	139	0.86	0.96	0.89	1.25
TDCO versus CFCO (pooled data)	251	0.87	0.85	0.89	0.99

CFCO = continuous Fick, EMCO = electromagnetic, TDCO = thermodilution cardiac output, r = correlation coefficient, SEE = standard error of the estimate. (*Adapted from* Goodyer AVN, Huvos A, Eckhardt WF, et al: Thermal dilution curves in the intact animal. Circ Res 7:432, 1959.)

correlation between the two techniques was good ($r = 0.86$) they noted that the Fick results were consistently lower than the thermodilution measurements.

Cardiac output has recently also been measured in humans by a Fick method that utilizes a computerized system for measuring oxygen consumption and carbon dioxide production.[7] Cardiac outputs determined with this system were compared with thermodilution measurements in intubated patients. A good correlation ($r = 0.92$) was observed between the two systems, indicating that the accuracy of the technique was high. More noteworthy was that the Fick measurements were more reproducible than the thermodilution measurements (the average standard deviation was 195 $\text{ml} \cdot \text{min}^{-1}$ for Fick, versus 1020 $\text{ml} \cdot \text{min}^{-1}$ for thermodilution).

INDICATOR DILUTION

The indicator-dilution technique is widely used today for the measurement of cardiac output. While its principle is based on the Fick principle, it differs from direct Fick in that a substance is injected into the circulation and its arrival is measured at a downstream point. Over the years an amazing variety of substances including water, methylene blue, and tetanus antitoxin have been injected into the circulation in an attempt to measure cardiac output. The first really meaningful experiments, however, were performed by Stewart (1860 to 1930) in the late nineteenth century.[62] He injected hypertonic saline solution (1.5 to 4.0 per cent) intravenously into anesthetized animals and detected the arrival of this indicator at arterial and venous sampling sites by observing the change in electrical conductance of the flowing blood. He recognized the change in electrical conductance by listening to a telephone circuit attached to a Wheatstone bridge.

Credit for the first measurement of cardiac output, in man, by injection of a foreign substance must be given to Hamilton (1893 to 1964). In 1932, he published his results obtained after injection of brilliant red and detection of this indicator by visual colorimetry.[25] In recognition for these two pioneers' contribution to the field of hemodynamic measurement, the equation used to calculate cardiac output by indicator dilution is now known as the Stewart-Hamilton equation.

Principles of the Measurement

The indicator-dilution theory is based on the observation that, for a known amount of indicator introduced at one point in the circulation, a same amount of indicator should be detectable at a downstream point. Stewart and Hamilton established that the amount of indicator detected at the downstream point was equal to the product of the cardiac output and the change in indicator concentration over time. Cardiac output is therefore calculated using the following equation:

$$CO = \frac{I \times 60}{\int_0^\infty Cdt}$$

where CO = cardiac output ($L \cdot min^{-1}$), I = amount of indicator injected (mg), C = concentration of indicator ($mg \cdot L^{-1}$), t = time (sec), 60 = 60 seconds per minute.

If the indicator is injected as a bolus, a recording of the indicator concentration over time will produce a bell-shaped curve. The area under the curve represents the denominator in the Stewart-Hamilton equation, and cardiac output is thus equal to the amount of injected indicator divided by the area under the curve. In other words, cardiac output is inversely proportional to the area under the curve.

In initial experiments, considerable difficulties were encountered in the selection of an ideal indicator. An ideal indicator is a substance that is easily detectable when mixed with blood, is water-soluble, nontoxic, and neither lost nor metabolized once it is in the blood during the sampling period. Indicators that have been used include various gases, dyes, and cold solutions. When dye indicators are used, the detection of the indicator is performed by a photoelectric device called a cuvette densitometer. This instrument consists of a variable light source and a light pathway through which blood from an arterial source is withdrawn at a constant rate. During passage of the blood, the electrical output of the cuvette densitometer is proportional to the concentration of the dye in the blood. As the dye concentration increases, more light is absorbed by the blood.

Early dyes were blue dyes with peak light absorption between 600 and 700 nm. In this spectral range, the cuvette could not distinguish between the dye and reduced hemoglobin. This often led to significant problems, particularly when cardiac output determinations were attempted in children with cyanotic heart disease. Fortunately, in 1957 Fox and his colleagues at the Mayo Clinic introduced indocyanine green, a dye with a peak absorption at 805 nm.[20] At 805 nm, the absorption of light by oxygenated and reduced hemoglobin is identical, and therefore, their relative concentrations become irrelevant. Indocyanine green is nontoxic, is rapidly removed from the circulation by the liver, and has a half-life in the circulation of approximately 10 minutes. Cardiac output determinations can be repeated, but plasma dye concentration gradually builds up. In clinical practice, it is common to inject 5 mg of indocyanine green into a central vein and to continuously sample arterial blood from a radial arterial catheter. The blood is passed through the cuvette densitometer and the change in indicator concentration over time is measured. A computer calculates the area under the dye concentration curve by integration of the dye concentrations and computes the cardiac output. The sampled blood is returned to the patient after completion of the cardiac output determination.

The idea of a thermal indicator was first introduced by Fegler in 1954.[17] He showed, in dogs, that the bolus injection of a cold solution resulted in a typical time-concentration curve and that the principles, developed by Stewart and Hamilton, could be used for the determination of cardiac output by injection of a thermal indicator. In his original publication, Fegler concluded that the thermodilution method was more flexible than the dye dilution method and allowed a greater number of measurements to be made.

In man, the first report on the use of thermodilution cardiac output measurements was published by Branthwaite and Bradley in 1968.[6] These investigators mounted a thermistor on a long nylon catheter and guided this catheter into the pulmonary artery. A second, shorter catheter was then introduced in the jugular vein and advanced until its tip was positioned near the junction of the superior vena cava and the right atrium. Thermal curves were recorded from the pulmonary artery following injection into the right atrium of 10 ml of 5 per cent dextrose at room temperature. One problem with this technique was the requirement of placing a thermistor in the pulmonary artery. The reason for positioning the thermistor in the pulmonary artery, rather than in a systemic vessel, was that previous work had demonstrated that during the first passage of the cold bolus, considerable amounts of the indicator were absorbed by the heart and lung tissue. Since this indicator was then gradually released, the return to baseline of the thermistor temperature was prolonged, introducing substantial error into the cardiac output calculations. With the subsequent development of the balloon-tipped, flow-directed pulmonary arterial catheter, placement of the catheter in the pulmonary artery became simple and today, in clinical practice, cardiac output is most commonly measured by the thermodilution technique.[19,63]

For the measurement of cardiac output by thermodilution, the Stewart-Hamilton equation needs to be modified to take the particular characteristics of the thermal indicator into account. It then becomes

$$\mathrm{CO} = \frac{V(T_B - T_I) \times K_1 \times K_2}{\int_0^\infty \Delta T_B(t)dt}$$

where CO = cardiac output ($\mathrm{L \cdot min^{-1}}$), V = volume of injectate (ml), T_B = initial blood temperature (°C), T_I = initial injectate temperature (°C), K_1 = density factor, K_2 = computation constant, which takes catheter dead space, heat change in transit, injection rate, and units into account, and $\int_0^\infty \Delta T_B(t)dt$ = integral of blood temperature change.

Accuracy and Precision

Accuracy. The accuracy of the thermodilution technique has been evaluated by comparing its results with those obtained by other methods of cardiac output determination, either in vitro or in vivo.

In vitro, a variety of mechanical models have been used to produce precisely controlled blood flows. In one such experiment, Salgado and Galetti[53] constructed a sophisticated system in which various determinants of cardiac output such as heart rate, stroke volume, and end-diastolic volume could be altered. They then compared the selected flows with thermodilution cardiac output measurements. In 139 measurements, with stroke volumes varying from 19 to 60 ml, the thermodilution outputs were found to be on average 2.9 per cent higher than the true flows. The overall standard deviation was ± 7 per cent. Bilfinger et al[5] performed similar measurements using commercially available pulmonary arterial catheters and cardiac output computers. They performed a total of 420 measurements at flow rates varying between 1.36 and 4.65 L per minute using 3, 5, and 10 ml injectate volumes at room temperature or ice cold. The average percentage differences between the thermodilution measurements and the reference values were 7 to 8 per cent at room temperature, and 11 to 13 per cent with ice cold saline. For single determinations the differences reached 15 to 25 per cent.

Thus, under strictly controlled, in vitro conditions the accuracy of the thermodilution cardiac output measurements varies from ±7 to ±13 per cent.

In vivo, the accuracy of the thermodilution technique has been tested in comparisons with the direct Fick method, electromagnetic flow measurements, and the indocyanine green method in numerous experiments.[38] When thermodilution measurements were compared with the direct Fick method, identical correlation coefficients of 0.96 per cent were obtained in two studies.[21,45] Pelletier[47] compared total electromagnetic flow, including coronary flow, with thermodilution cardiac output in dogs. He observed that, on average, thermodilution overestimated total aortic flow by ±3 per cent, whether iced or room temperature injectate was used.

The most common comparisons have been between thermodilution and indocyanine green. The results have varied between various studies, with some authors finding excellent correlations over a wide range of outputs, while others observe that thermodilution systematically overestimates dye cardiac output.[52,58,70] One should remember, however, that both of these techniques are based on the same principle and that the accuracy of both is contingent on a large number of conditions being met. Indeed, for the duration of the measurements (1) the flow must be constant, (2) the blood volume must be constant, (3) the indicator must not recirculate, (4) there must not be any stagnant pools, (5) the distribution of traversal times of the indicator must not change with time, and (6) the flow of the indicator particles must be representative of the total flow.[5] Under clinical circumstances, it is unusual for all of these conditions to be satisfied. Whether the discrepancies between the dye technique and thermodilution are attributed to inaccuracies in one or the other technique often depends on the author's convictions. In general, however, it is accepted that, under optimal circumstances, the error in accuracy of the thermodilution cardiac output technique is ±10 per cent.

Factors That Influence the Accuracy. The accuracy figures cited previously are valid only if the thermodilution measurements are performed with an optimal technique. Numerous operator errors can occur, and they will affect the accuracy of the measurements. It is, for instance, important to remember that once the computation constant has been entered, the cardiac output computer will base its calculations on a very specific volume of indicator, at a very specific temperature. If the delivered amount of indicator is smaller than the volume for which the cardiac computer has been programmed, the cardiac output value will be erroneously elevated. A measurement error will occur if, for example, the computation constant for 10 ml of injectate at 0°C was entered, but the actual injectate temperature was 10°C. The amount of injected indicator will be less than expected and the measured cardiac output will be greater than the true cardiac output. This type of error is particularly likely when iced indicator is used. At room temperature, an iced syringe held by the plunger will increase in temperature at a rate of 1 to 2°C per minute. If it is held tightly in the palm of the hand, the temperature will rise at 4 to 5°C per minute. For each increase in injectate temperature of 1°C, the cardiac output will be overestimated by 3 per cent. For this reason, when using iced indicator, the temperature should be measured as close to the injectate site as possible. In many centers only room temperature indicator is used.

Similar errors occur when the volume of the indicator does not correspond to the volume indicated by the computation constant. Loss of volume occurs when the syringes are incompletely filled, or when the proximal injection port of the pulmonary artery catheter is located within the introducer sheath. Injection in this location will result in loss of indicator to the side arm of the introducer and falsely elevated cardiac output values.

The opposite will be observed when more indicator is delivered than the computer was programmed for. Recently, Wetzel et al[71] observed variations, of up to 80 per cent, in measured cardiac output when the rate of administration of room temperature peripheral crystalloid infusions was intermittently and rapidly altered. Under those circumstances, the errors were due to fluctuations in baseline blood temperature (Figs. 2 and 3).

Other errors are occasionally observed in the presence of unusual conditions within the circulation. For instance, in patients with intracardiac shunts the cardiac output cannot be measured by the thermodilution technique. Rapid recirculation will result in loss of indicator and erroneously elevated values. Kahan et al[34] recently reported a case in which very elevated cardiac output values were measured, although the patient was clinically in cardiogenic shock. The error was due to an aortopulmonary fistula.

Precision. As mentioned in the introduction, the precision or reproducibility of a technique will markedly influence its clinical applicability and the manner in which it is utilized for clinical decision making. The reproducibility of the thermodilution method has also been tested in vivo and in vitro.

In vitro, Mackenzie et al[39] have compared thermodilution cardiac output measurements with absolute flows measured in an artificial circulation. The thermodilution measurements were obtained with cardiac output computers (IL 701, Lexington, MA; Edwards 9520A, Santa Ana, CA; and Gould SP1435, Oxnard, CA) from three different manufacturers. The authors calculated linear regressions between the actual flow and the measured cardiac output, at several flow rates and with various injectate volumes and temperatures. For each linear regression they calculated the predicted cardiac output measurement at a fixed flow of 5 $L \cdot min^{-1}$, as well as the 95 per cent confidence interval for this predicted measurement. The value of the 95 per cent confidence interval represented the range of flow rates that could have given rise to an identical measurement. For the studied computers, they were 2.0, 1.5, and 3.1 $L \cdot min^{-1}$, respectively. The authors concluded that the reproducibility of the computers' results was poor and that their ability to detect changes in flow rates was limited.

In vivo, reproducibility can be assessed by obtaining a large number of thermodilution cardiac outputs and calculating their standard deviation. Hoel[30] published such a study in 1978. He first obtained 573 thermodilution determinations and calculated that their standard deviation was 5.1 per cent. He then postulated that a true cardiac output could be measured by calculating the average of an infinite number of thermal injections. Using probability calculus he derived that with two injections there was only a 50 per cent probability to be within 5 per cent of the true cardiac output. To reach a 95 per cent probability to be within 5 per cent of the true cardiac output would require seven injections (Table 2). With three injections there was an 89 per cent probability to within 10 per cent of the true cardiac output.

In an attempt to better delineate the reproducibility of the technique, Stetz et al[60] reviewed 14 publications on the use of thermodilution in clinical practice. They concluded that with the use of commercial thermodilution devices, a minimal difference of 12 to 15 per cent (average 13 per cent) between determinations is required to be statistically significant, provided that each determination was obtained by averaging three measurements. If each determination was the result of only a single measurement, a minimal difference of 20 to 26 per cent (average 22 per cent) was required for statistical significance. They also noted that the thermodilution, direct Fick, and in-

Table 2. *Reproducibility of Thermodilution*

NO. OF INJECTIONS	±10%	±5%
2	70%	49%
3	89%	70%
4	96%	81%
5	98%	87%
6		92%
7		95%
8		96%

Per cent probability that cardiac output based on n thermodilution (TD) curves will lie within ±10% or ±5% of cardiac output based on an infinite number of TD curves. (*Adapted from* Hoel BL: Some aspects of the clinical use of thermodilution in measuring cardiac output. Scand J Clin Invest 38:383, 1978.)

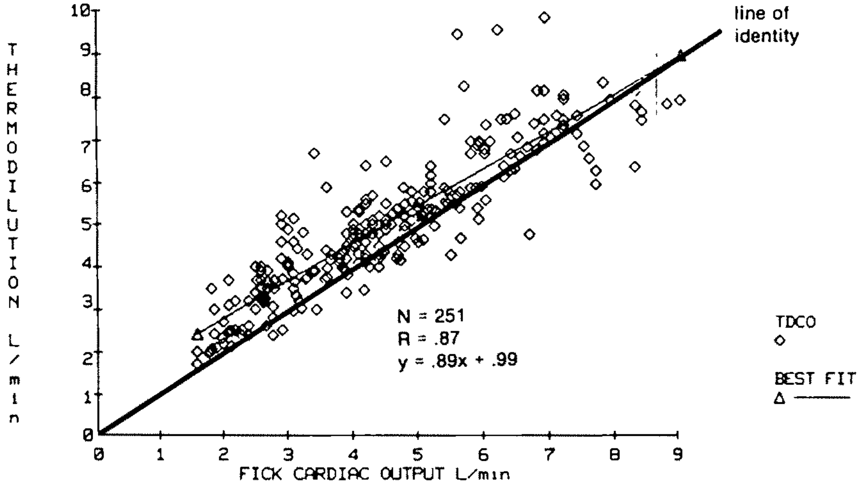


Figure 1. Thermodilution versus continuous Fick cardiac output. (*From* Davies G, Hess D, Jebson P: Continuous Fick cardiac output compared to continuous pulmonary artery electromagnetic flow measurements in pigs. Anesthesiology 66:805, 1987; with permission.)

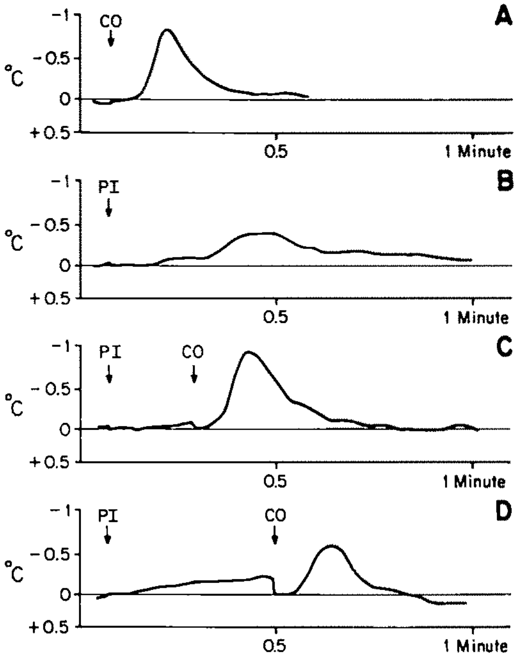
docyanine green were equally accurate, and that the accuracy was not influenced by the use of iced versus room temperature indicator.

A few studies have also evaluated the effects of the timing of the injection in the respiratory cycle on the reproducibility of thermodilution cardiac output. In mechanically ventilated dogs, Snyder and Powner[57] injected indicator at sequential, 1-second intervals within the respiratory cycle. They noted that cardiac output variations were present in each respiratory cycle and were usually greater than 10 per cent. They postulated that these variations were reflections of changes in flow induced by respiration, rather than random artifacts. Indocyanine green cardiac outputs were less affected by the respiration. The authors concluded that the injection of thermal indicator, at a specific moment in the respiratory cycle, improved the reproducibility of the measurement but could result in a systematic error.

Stevens et al[61] have studied the effects of the respiratory cycle on thermodilution cardiac output in critically ill patients. They prospectively studied 32 patients in a randomized scheme comparing three thermodilution cardiac output measurements at peak-inspiration, at end-exhalation, or randomly in spontaneously breathing and mechanically ventilated patients. These investigators confirmed that injections at specific times in the respiratory cycle resulted in less variability, but possibly decreased accuracy. They nevertheless concluded that, in clinical practice, the improvement in reproducibility was more important than the decrease in accuracy.

The effects of injectate volume and temperature on the variability of thermodilution cardiac output have also been studied in critically ill patients.[46] Six combinations of injectate volume (3, 5, and 10 ml) and temperature (0°C and room temperature) were studied in 18 adult,

Figure 2. Temperature curves from thermodilution output computer. CO = start of cardiac output measurement (followed by injection of iced saline); PI = start of peripheral volume infusion. A, Normal curve (TCDO = 3.21 L/min). B, Curve from peripheral volume infusion alone. C, Injection of iced saline just after start of peripheral volume infusion (TDCO = 2.18 L/min). D, Injection of iced saline approximately 20 s after peripheral volume infusion (TDCO = 4.52 L/min). (*From* Wetzel RC, Latson TW: Major events in thermodilution cardiac output measurement during rapid volume infusion. Anesthesiology 62:684, 1985; with permission.)



intubated patients. The best reproducibility was obtained with the 10-ml injections at 0°C or room temperature.

In summary, the precision of the thermodilution cardiac output technique is not very good and every attempt should be made to improve it. For each determination, the rate and duration of the injection should be kept as constant as possible. An injector gun can be useful for this purpose.[43] Whenever possible, 10-ml volumes of injectate should be used and the timing of the injection in the respiratory cycle should be the same. However, by keeping the timing of the injections constant in the respiratory cycle, some loss in accuracy is to be expected.

Limitations

The dye dilution method has several limitations. The preparation of the indicator solution is tedious and time consuming, and the calibration of the cuvette densitometer is an intricate procedure. Indocyanine green is a relatively unstable substance, particularly in solution. The technique requires blood withdrawal, which makes it complex and cumbersome, and also renders rapid and sequential measurements impossible. Recirculation of the indicator distorts the primary time-concentration curve, necessitating extrapolation of the downslope. Finally, the build up of indicator in the blood results in high background concentration and limits the total number of measurements that can be obtained.

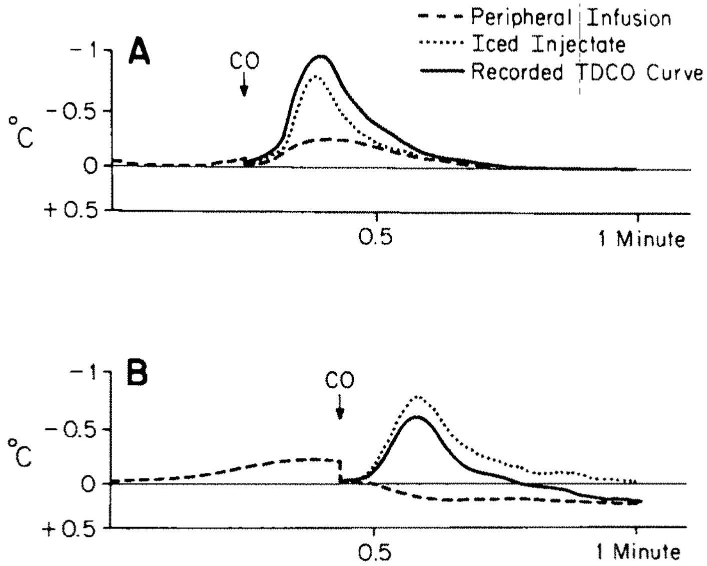


Figure 3. Diagramatic representation of effects of peripheral volume infusion on temperature curve. Peripheral volume infusion was started at time = 0. CO = start of cardiac output measurement (followed by iced saline injection). A, Temperature change caused by peripheral volume infusion augments measured change following iced saline injection. B, Temperature change caused by volume infusion decreases measured change following iced saline injection (notice effect of "rezeroing" referenced baseline temperature at CO). (*From* Wetzel RC, Latson TW: Major errors in thermodilution cardiac output measurement during rapid volume infusion. Anesthesiology 62:684, 1985; with permission.)

The use of thermal indicator has eliminated some, but not all, of these limitations. Handling the indicator is undoubtedly easier with thermal than with dye indicator. The computer calibration procedures are greatly simplified and blood withdrawal is not necessary. Some common problems, however, remain. Extrapolation of the tail end of the time-concentration curve remains essential. Various manufacturers have handled this problem differently, and inconsistencies can sometimes be observed when switching from one computer to another.[40]

Pulmonary artery catheterization is not without problems and the list of reported complications is long. Additionally, the determination of cardiac output remains intermittent and frequent measurements can lead to fluid overload. Complications have also been attributed to the rapid injection of cold indicator into the right atrium. Slowing of the heart rate was described by Nishikawa and Dohi[44] In a prospective study, Harris et al[27] observed that, with the use of iced injectate, a decrease in heart rate of more than 10 per cent occurred in 22 per cent of the determinations.

Finally, the presence of shunts between the cardiac chambers or major vessels will interfere with cardiac output determinations using either dye or thermal indicator.

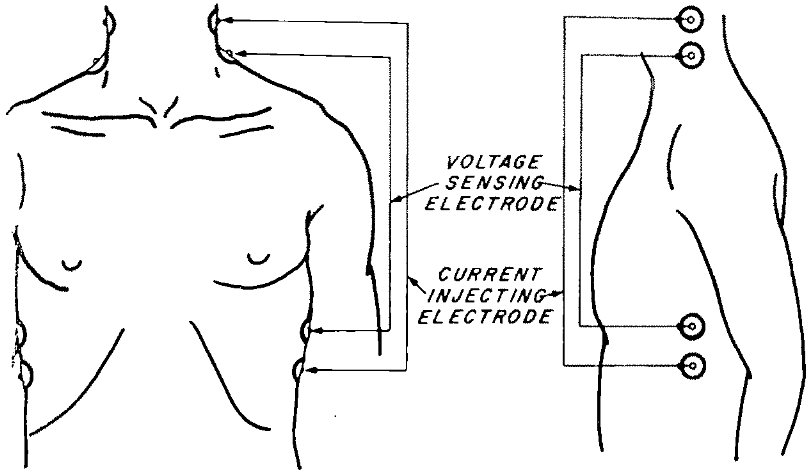


Figure 4. Proper placement of the eight spot surface electrode array. (*From* Bernstein DP: Continuous nonivasive real-time monitoring of stroke volume and cardiac output by thoracic electrical bioimpedance. Crit Care Med 14:898, 1986; with permission.)

Recent Developments

Fiberoptic Dye Detection. In recent years, an earpiece densitometer has been developed for the measurement of cardiac output by dye dilution.[51] The earpiece alleviates the need for arterial blood sampling and therefore greatly simplifies the measurement technique. The earpiece contains a light source, and inflatable rubber diaphragm, and two phototransistors (805 and 900 nm). The dye concentratiuon in the blood is computed from the change in light absorption, measured with the phototransistors. The results obtained with this technique have been compared with conventional dye dilution and thermodilution.[22,49,64] Some investigators have found excellent correaltions, while others were not as successful. The reproducibilty of the earpiece method has been found comparable to that of thermodilution. The quality of the results appears to be determined by patient selection, the judicious rejection of unsuitable curves, and the site of indicator injection.

Another recent design consists of a fiberoptic catheter for the determination of oxygen saturation, as well as dye concentration. The catheter appears most useful in children who have undergone surgical correction of congenital heart disease. It is placed in the pulmonary artery at the time of surgery and allows continuous monitoring of mixed venous saturation, with intermittent measurements of dye cardiac outputs, without arterial blood sampling.

Continuous Thermal Cardiac Output. Early in the development of the thermodilution method, attempts were made at providing a continuous thermal signal and therefore a continuous cardiac output determination. The initial experiments were focused on the use of

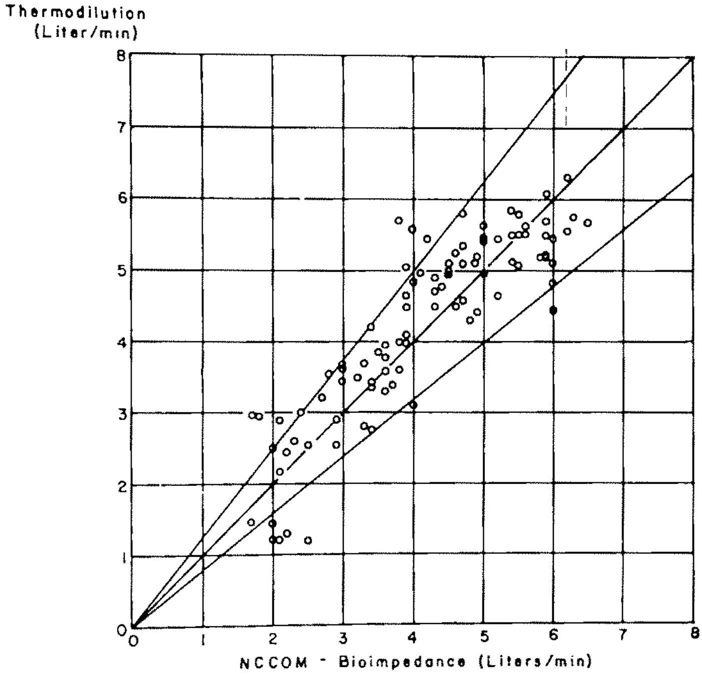


Figure 5. Scattergram showing comparison between Q_{teb} (horizontal axis) and Q_{td} (vertical axis). Limits defining 20 per cent variability from the identity line are shown ($r = 0.88$; $y = 0.86x + 0.65$). (*From* Bernstein DP: Continuous noninvasive real-time monitoring of stroke volume and cardiac output by thoracic electrical bioimpedance. Crit Care Med 14:898, 1986; with permission.)

intravascular heating devices.[2,35] However, because heating blood is more dangerous than cooling it, the use of heating devices was inherently more risky. As a result, very low amplitude heat signals needed to be used, and separation of the introduced heat signal from background thermal variations became a major problem. More recently, Philip et al[48] have again explored the possibility of a continuous thermal signal using a very low power (5 W) sinusoidal thermal signal. With this system the average increase in blood temperature was only of the order of 0.02°C at typical flows. They tested the system both in vitro and in vivo and obtained satisfactory correlations with conventional thermodilution over a wide range of cardiac outputs.

OTHER TECHNIQUES

Pulse Contour

The notion that stroke volume can be quantified from the pulse pressure dates back to observations by Erlanger and Hooker in 1904. Since then, numerous techniques have been described to calculate stroke volume from a central aortic arterial pulse recording. In a critical review of these many pulse pressure methods, Kouchoukos et al[36] found an overall correlation coefficient of 0.928 with a standard error of the estimate of 17.4 per cent for Warner's method.

All the pulse contour methods are based on the same formula:

$$\text{Stroke volume} = K \int_0^\infty \{P(t) - PED\}dt$$

where K = a constant, $\{P(t) - PED\}dt$ = the difference between the actual pressure P(t) and the end-diastolic pressure PED over time dt.[50]

The various methods differ only in the determination of the constant K. In Warner's formula K is

$$K = F(1 + T_s/T_d)$$

where F = a factor relating the calculated stroke volume to a stroke volume measured with another technique, T_s = the duration of systolic ejection, and T_d = the duration of diastole.

Recently, English et al[14] have assessed the accuracy and reproducibility of cardiac output measurements by computer analysis of the aortic pressure wave (Warner's method) in halothane-anesthetized dogs. They obtained more than 800 simultaneous cardiac output determinations using the pulse wave and thermodilution methods, at various halothane concentrations (0.5 to 2.0 per cent) and various systemic vascular resistances. Good correlations ($r = 0.91$ or better) between the two techniques were noted at all halothane concentrations, irrespective of the systemic vascular resistance. However, they observed a marked deterioration in correlations ($r < 0.5$) when systemic vascular resistance was altered by more than 50 per cent, using phenylephrine or sodium nitroprusside.

Systolic Time Intervals

Systolic time intervals measure the duration of various events in left ventricular systole and are obtained by simultaneous recordings of the ECG, the phonocardiogram, and the systemic arterial pressure. Total electromechanical systole (QS_2) is the interval from the onset of the QRS complex to the first major deflection of the second heart sound. The left ventricular ejection time (LVET) is measured from the arterial upstroke to the dicrotic notch. The pre-ejection period (PEP) is equal to the difference between the LVET and QS_2. Steinberg et al[59] studied the correlation between the systolic time intervals and stroke volume, measured by thermodilution, in animals and man. They found that the difference between LVET and PEP yielded the best correlations with thermodilution stroke volumes. However, large variabilities were observed in the systolic time intervals of individual patients, complicating the comparison among patients of stroke volumes derived from these intervals.

Ultrasound

Ultrasound can be used in a variety of ways to measure stroke volume and cardiac output. M-mode echocardiography can be utilized to measure systolic time intervals. Both M-mode and two-dimensional echocardiography can be used to measure ventricular dimensions and to derive ventricular volumes. Using an epicardial two-dimensional echo transducer and single plane short-axis views, we obtained a good correlation ($r = 0.80$) between echo-derived and thermodilution cardiac output.[66]

Another approach to the use of ultrasound for the measurement of cardiac output is based on the Doppler principle. Doppler frequency shifts can be detected at the cardiac valves, or in the major vessels. The ultrasound signals can be emitted and detected with transthoracic transducers, esophageal transducers, implantable crystals, or catheter-mounted crystals. For details on the principle of the measurements and results of published studies, the reader is referred to the preceding articles.

Laser Doppler Velocimetry

Laser Doppler velocimetry uses the Doppler shift of laser light to measure cutaneous blood flow. The laser light is reflected off the red blood cells in the cutaneous capillaries, and the frequency shift resulting from this reflection quantitates the red blood cell flow. Early animal experiments suggested that cutaneous laser Doppler velocimetry accurately reflects changes in cardiac output.[69] In critically ill patients, Waxman et al[68] observed that the laser probes reflected acute directional changes in cardiac output and that with heated probes the magnitude of the changes was also reflected. However, they concluded that absolute values of laser Doppler velocimetry are not predictive of absolute cardiac output values. In a different study, Eyer et al[16] came to the same conclusions.

Thoracic Electrical Impedance

The first attempts at measuring cardiac output by thoracic electrical impedance date back to 1966, when Kubicek et al[37] presented an empiric equation for the calculation of left ventricular stroke volume. Electrical impedance (Z) is the resistance to alternating or sinusoidal current flow. It is a complex, frequency-dependent parameter that is governed by Ohm's law:

$$Z = E/I$$

where Z = impedance in ohms, E = voltage, and I = current in amperes.

To measure thoracic electrical impedance, an alternating current of low amplitude and high frequency is introduced and simultaneously sensed by two sets of electrodes placed around the neck and lower thorax (Fig. 4). Changes in thoracic impedance are induced by the ventilation and the pulsatile blood flow. For the measurement of cardiac output, only the cardiac-induced pulsatile component is analyzed (δZ). Experimental work suggests that 70 to 80 per cent of δZ originates from the thoracic aorta. To quantitate Z, it is assumed that the thorax is a perfectly circular cylinder of length L (cm) and cross-sectional area A (cm^2). For cylindrical volume conductions

$$Z = \rho \frac{L}{A}$$

where ρ = specific resistivity of the electrical conductor ($\Omega \cdot cm$).

Stroke volume is calculated with the empirical formula of Kubicek:

$$SV = \rho \times \left(\frac{L}{Z_0}\right) \times LVET \times \left(\frac{\delta Z}{\delta t_{max}}\right)$$

where ρ = the resistivity of blood at 100 kHz ($\Omega \cdot cm$), L = distance between the two inner electrodes (cm), Z_0 = the base impedance (Ω), LVET = the left ventricular ejection time (sec), and $\delta Z/\delta t_{max}$ = the maximum rate of change in impedance during systole (Ω per second).

Donovan et al[11] recently compared cardiac output measurements obtained by transthoracic impedance and by thermodilution in 27 critically ill patients, using the standard Kubicek equation. Although they attempted to solve the equation with multiple values for the distance between the inner electrodes and for the resistivity of blood, they did not find a satisfactory correlation between the two cardiac output methods. Bernstein[3] has modified the Kubicek equation by eliminating the specific resistance of blood, modeling the thorax as a truncated cone instead of a cylinder, incorporating a constant relating the patient's height, rather than the distance between the electrodes, into the equation, and, finally, adjusting this constant to ideal body weight. In 17 critically ill patients, he obtained 94 simultaneous thoracic electrical impedance and thermodilution cardiac outputs (Fig. 5).[4] The overall correlation between the two techniques was good ($r = 0.88$) and 85 per cent of the data points fell within the 20 per cent confidence limits. The greatest disparity between the two techniques was observed at very low flows ($<2\ L \cdot min^{-1}$).

Appel et al,[1] using a device that incorporates the Bernstein modifications, have also compared cardiac output by thoracic electrical impedance and thermodilution in 16 critically ill patients. They compared 391 pairs of simultaneous cardiac outputs and found an r value of 0.83. The Bernstein modifications, thus, appear to improve the accuracy of the bioimpedance method, but additional studies will be required to identify and quantitate the limitations of the technique. Nonetheless, these recent developments in thoracic bioimpedance technology suggest that, in the future, it may play a considerable role in the noninvasive monitoring of cardiac output in the surgical patient.[67]

SUMMARY

Numerous techniques are currently available for the measurement of cardiac output in the operating room. While the direct Fick method is often considered the gold standard, it has not been widely used in the surgical patient. With the recent widespread availability of mass spectrometry and continuous hemoglobin oximetry, it could become more popular again. The thermodilution technique is most commonly used to measure cardiac output in clinical practice, although its accuracy and reproducibility are not great. At least three consistent thermodilution determinations are required for an accurate cardiac output measurement. Errors will occur when indicator is lost or gained, while an inconsistent injection technique will produce variability in the results. New noninvasive methods to measure cardiac output are very promising. They include the Doppler technique and the thoracic bioimpedance method. In this last method, the thoracic electrical impedance is measured by sets of electrodes placed around the neck and lower thorax. The latest bioimpedance equipment incorporates new equations that have increased the accuracy of the technique.

REFERENCES

1. Appel PL, Kram HB, Mackabee J, et al: Comparison of measurements of cardiac output by bioimpedance and thermodilution in severely ill surgical patients. Crit Care Med 14:933, 1986
2. Barankay T, Jansco T, Nagay S, et al: Cardiac output estimation by a thermodilution method involving intravascular heating and thermistor recording. Acta Physiol Acad Sci Hungariae 38:167, 1970
3. Bernstein DP: A new stroke volume equation for thoracic electrical bioimpedance: Theory and rationale. Crit Care Med 14:904, 1986
4. Bernstein DP: Continuous noninvasive real-time monitoring of stroke volume and cardiac output by thoracic electrical bioimpedance. Crit Care Med 14:898, 1986
5. Bilfinger TV, Lin CY, Anagnostopoulos CE: In vitro determination of accuracy of cardiac output measurements by thermal dilution. J Surg Res 33:409, 1982
6. Branthwaite MA, Bradley RD: Measurement of cardiac output by thermal dilution in man. J Appl Physiol 24:434, 1968
7. Carpenter JP, Nair S, Staw I: Cardiac output determination: Thermodilution versus a new computerized Fick method. Crit Care Med 13:576, 1985
8. Cross KW, Groom AC, Mottram RF, et al: Cardiac output in the cat: A comparison between the Fick method and a radioactive indicator dilution method. J Physiol 136:24P, 1957
9. Davies G, Hess D, Jebson P: Continuous Fick cardiac output compared to continuous pulmonary artery electromagnetic flow measurements in pigs. Anesthesiology 66:805, 1987
10. Davies GG, Jebson PJR, Glasgow BM, et al: Continuous Fick cardiac output compared to thermodilution cardiac output. Crit Care Med 14:881, 1986
11. Donovan KD, Dobb GJ, Woods WPD, et al: Comparison of transthoracic electrical impedance and thermodilution methods for measuring cardiac output. Crit Care Med 14:1038, 1986
12. Doyle JT, Wilson JS, Lepine C, et al: An evaluation of the measurement of the cardiac output and of the so-called pulmonary blood volume by the dye dilution method. J Lab Clin Med 41:29, 1953

13. Eliasch H, Lagerlöf H, Bucht H, et al: Comparison of the dye dilution and the direct Fick methods for the measurement of cardiac output in man. Scand J Clin Lab Invest 7(suppl 20):73, 1955
14. English JB, Hodges MR, Sentker C, et al: Comparison of aortic pulse-wave contour analysis and thermodilution methods of measuring cardiac output during anesthesia in the dog. Anesthesiology 52:56, 1980
15. Etsten B, Li TH: The determination of cardiac output by the dye dilution method: Modifications, comparison with the Fick method, and application during anesthesia. Anesthesiology 15:217, 1954
16. Eyer S, Borgos J, Strate RG: Laser Doppler flowmetry and cardiac output in critically ill surgical patients. Crit Care Med 15:778, 1987
17. Fegler G: Measurement of cardiac output in anesthetized animals by a thermodilution method. Q J Exp Physiol 39:153, 1954
18. Fick A: Über die Messung des Blutquantums in den Herzventrikeln. Sitz Physik Med Würzburg, 1870, p 16
19. Forrester JS, Ganz W, Diamond G, et al: Thermodilution cardiac output determination with a single flow-directed catheter. Am Heart J 83:306, 1972
20. Fox IJ, Brooker QS, Heseltine DW, et al: A tricarbocyanine dye for continuous recording of dilution curves in whole blood independent of variations in blood oxygen saturation. Proc Staff Meetings Mayo Clin 32:478, 1957
21. Goodyer AVN, Huvos A, Eckhardt WF, et al: Thermal dilution curves in the intact animal. Circ Res 7:432, 1959
22. Grasberger RC, Yeston NS: Less-invasive cardiac output monitoring by earpiece densitometry. Crit Care Med 14:577, 1986
23. Grossman W: Fick oxygen method. *In* Cardiac Catheterization and Angiography, ed 2. Philadelphia, Lea & Febiger, 1986, p 105
24. Guyton AC: The Fick principle. *In* Guyton AC, Jones CE, Coleman TG (eds): Circulation Physiology: Cardiac Output and Its Regulation, ed 2. Philadelphia, W.B. Saunders, 1973, p 21
25. Hamilton WF, Moore JW, Kinsman JM, et al: Studies on the circulation. IV. Further analysis of the injection method, and changes in hemodynamics under physiological and pathological conditions. Am J Physiol 99:534, 1932
26. Hamilton WF, Riley RL, Attyah AM, et al: Comparison of Fick and dye injection methods of measuring cardiac output in man. Am J Physiol 153:309, 1948
27. Harris AP, Miller CF, Beattie C, et al: The slowing of sinus rhythm during thermodilution cardiac output determination and the effect of altering injectate temperature. Anesthesiology 63:540, 1985
28. Heneghan CPH, Brantwaithe MA. Non-invasive measurement of cardiac output during anaesthesia. Br J Anaesth 53:351, 1981
29. Heneghan CPH, Gillbe CE, Brantwaithe MA: Measurement of metabolic gas exchange during anaesthesia. Br J Anaesth 53:73, 1981
30. Hoel BL: Some aspects of the clinical use of thermodilution in measuring cardiac output. Scand J Clin Lab Invest 38:383, 1978
31. Howell CD, Horvath SM: Reproducibility of cardiac output measurements in the dog. J Appl Physiol 14:421, 1959
32. Huggins RA, Smith EL, Sinclair MA: Comparison between the cardiac output measured with a rotameter and output determined by the direct Fick method in open-chest dogs. Am J Physiol 160:183, 1950
33. Jurado RA: Measurement of cardiac output by the direct Fick method. *In* Litwak RS, Jurado RA (eds): Care of the Cardiac Surgical Patient. Norwalk, CT, Appleton-Century-Crofts, 1982, p 495.
34. Kahan F, Profeta J, Thys DM: High cardiac output measurements in a patient with congestive heart failure. J Cardiothorac Anesth 1:234, 1987
35. Khalil HH, Richardson TQ, Guyton AC: Measurement of cardiac output by thermal dilution and direct Fick methods in dogs. J Appl Physiol 21:1131, 1966
36. Kouchoukos NT, Sheppard LC, McDonald DA, et al: Estimation of stroke volume from the central arterial pulse contour in postoperative patients. Surg Forum 20:180, 1969

37. Kubicek WG, Karegis JN, Patterson RP, et al: Development and evaluation of an impedance cardiac output system. Aerospace Med 37:1208, 1966
38. Levett JM, Replogle RL: Thermodilution cardiac output: A critical analysis and review of the literature. J Surg Res 27:392, 1979
39. Mackenzie JD, Haite NS, Rawles JM: Method of assessing the reproducibility of blood flow measurement: Factors affecting the performance of thermodilution cardiac output computers. Br Heart J 55:14, 1986
40. Matthew EB, Vender JS: Comparison of cardiac output measured by different computers. Crit Care Med 15:989, 1987
41. Milnor WR: Historical developments in hemodynamics. *In* Hemodynamics. Baltimore, Williams & Wilkins, 1982, p 4
42. Moore JW, Kinsman JM, Hamilton WF, et al: Studies on the circulation. II. Cardiac output determinations: Comparison of the injection method with the direct Fick procedure. Am J Physiol 89:331, 1929
43. Nelson LD, Houtchens BA: Automatic versus manual injections for thermodilution cardiac output determinations. Crit Care Med 10:190, 1982
44. Nishikawa T, Dohi S: Slowing of heart rate during cardiac output measurement by thermodilution. Anesthesiology 57:538, 1982
45. Pavek K, Lindquist O, Arfors KE: Validity of thermodilution method for measurement of cardiac output in pulmonary oedema. Cardiovasc Res 7:419, 1973
46. Pearl RG, Rosenthal MH, Nieson L, et al: Effect of injectate volume and temperature on thermodilution cardiac output determination. Anesthesiology 64:798, 1986
47. Pelletier C: Cardiac output measurement by thermodilution. Can J Surg 22:347, 1979
48. Philip JH, Long MC, Quinn MD, et al: Continuous thermal measurement of cardiac output. IEEE Trans Biomed Eng 31:393, 1984
49. Powner DJ, Dahl D, Shucker L: Ear densitometer cardiac outputs versus thermodilution outputs. Crit Care Med 12:148, 1984
50. Prys-Roberts C: Monitoring of the cardiovascular system. *In* Saidman LJ, Smith NT (eds): Monitoring in Anesthesia. New York, Wiley, 1978, p 62
51. Robinson PS, Crowther A, Jenkins BS, et al: A computerized dichromatic earpiece densitometer for the measurement of cardiac output. Cardiovasc Res 13:420, 1979
52. Runciman WB, Ilsly AH, Roberts JG: Thermodilution cardiac output—a systematic error. Anaesth Int Care 9:135, 1981
53. Salgado CR, Galletti PM: In vitro evaluation of the thermodilution technique for the measurement of ventricular stroke volume and end-diastolic volume. Cardiologia 49:65, 1966
54. Seely RD, Gregg DE: A technique for measuring cardiac output directly by cannulation of the pulmonary artery. Proc Soc Exp Biol Med 73:269, 1950
55. Seely RD, Nerlich WE, Gregg DE: Comparison of cardiac output determined by the Fick procedure and a direct method using the rotameter. Circulation 1:1261, 1950
56. Selzer A, Sudrann RB: Reliability of the determination of cardiac output in man by means of the Fick principle. Circ Res 6:485, 1958
57. Snyder JV, Powner DJ: Effects of mechanical ventilation on the measurement of the cardiac output by thermodilution. Crit Care Med 10:677, 1982
58. Sorensen MB, Bille-Brahe NE, Engell HC: Cardiac output measurement by thermodilution. Ann Surg 183:67, 1976
59. Steinberg R, Dauchot PJ: Noninvasive assessment of stroke volume by systolic time intervals. Anesthesiology 55:A36, 1981
60. Stetz CW, Miller RG, Kelly GE, et al: Reliability of the thermodilution method in the determination of cardiac output in clinical practice. Am Rev Respir Dis 126:1001, 1982
61. Stevens JH, Raffin TA, Mihm FG, et al: Thermodilution cardiac output measurement: Effects of the respiratory cycle on its reproducibility. JAMA 253:2240, 1985

62. Stewart GN: Researches on the circulation time and on the influences which affect it. IV. The output of the heart. J Physiol 22:159, 1897
63. Swan HJC, Ganz W, Forrester J, et al: Catheterization of the heart in man with use of a flow-directed balloon-tipped catheter. N Engl J Med 283:447, 1970
64. Tanner G, Barash PG: Cardiac output measured by earpiece densitometry vs. thermodilution. Crit Care Med 12:1082, 1984
65. Thomasson B: Cardiac output in normal subjects under standard basal conditions: The repeatability of measurements by the Fick method. Scand J Clin Lab Invest 9:365, 1957
66. Thys DM, Hillel Z, Goldman ME, et al: A comparison of hemodynamic indices derived by invasive monitoring and two-dimensional echocardiography. Anesthesiology 76:630, 1987
67. Tremper K: Continuous noninvasive cardiac output: Are we getting there? Crit Care Med 15:278, 1987
68. Waxman K, Formosa P, Sloiman H, et al: Laser Doppler velocimetry in critically ill patients. Crit Care Med 15:780, 1987
69. Waxman K, Police AM, Cheung CK, et al: Laser Doppler velocimetry as a monitor of cardiac output changes in dogs. Crit Care Med 13:194, 1985
70. Weisel RD, Berger RL, Hechtman HB, et al: Measurement of cardiac output by thermodilution. N Engl J Med 292:682, 1975
71. Wetzel RC, Latson TW: Major errors in thermodilution cardiac output measurement during rapid volume infusion. Anesthesiology 62:684, 1985
72. Wood EH, Bowers D, Shepherd JT, et al: O_2 content of mixed venous blood in man during various phases of the respiratory and cardiac output cycles in relation to possible errors in measurement of cardiac output by conventional applications of the Fick method. J Appl Physiol 215:605, 1968

Division of Cardiothoracic Anesthesiology
Department of Anesthesiology
Mount Sinai School of Medicine
One Gustave L. Levy Place
New York, NY 10029

0889-8537/88 $0.00 + .20

Cardiovascular Monitoring for the Pediatric Patient: What's Appropriate?

Paul Robert Hickey, MD, Dolly Doris Hansen, MD,† and Corrie Anderson, MD‡*

Two trends are apparent in cardiovascular monitoring for pediatric patients in the operating room. One, with more complex operations being performed on younger and sicker children, more sophisticated and immediate information about both the systemic and pulmonary circulations is required. The intimate relationship between pulmonary and cardiac function in young children and the frequent presence of an abnormal pulmonary circulation require more emphasis on monitoring of the pulmonary circulation. Development of noninvasive monitoring is the other important trend affecting pediatric cardiovascular monitoring. In small, fragile children, additional morbidity can result from the monitoring process itself. This is due to scale factors in downsizing adult monitors, low tolerance for malposition of monitoring devices in small anatomic structures, and different tissue characteristics present in small children. The appropriate selection of cardiovascular monitoring for children thus is not a trivial question nor one that can be easily extrapolated from experience in adults.

The appropriate monitoring for any given pediatric patient depends on the surgical procedure planned, the foreseeable complications, the preoperative condition of the child, and the anesthesiologist's experience with any particular monitoring modality. Clearly, use of invasive monitoring that carries appreciable risk cannot be justified unless the anesthesiologist has sufficient experience to minimize the associated risk *and* to use the resulting data correctly. Because there is little hard evidence of improved outcome as a result of invasive monitors, monitors must be used judiciously. By misleading the unwary clinician, even noninvasive monitors, when used incorrectly or when misinterpreted, can indirectly harm the patient. The purpose of this article is to present the different types of cardiovascu-

---

The Children's Hospital and Harvard Medical School, Boston, Massachusetts

*Associate Professor of Anaesthesia
†Assistant Professor of Anaesthesia
‡Clinical Fellow in Anaesthesia

lar monitoring available for pediatrics, the limitations of these monitors, and associated risks, and finally, to suggest situations in which specific types of monitoring may be useful in children.

BASIC NONINVASIVE MONITORING

Observation: The Anesthesiologist as Monitor

The senses of the anesthesiologist are the most reliable and simplest monitors. In small children, precise, invasive measurement of many physiologic variables is difficult and thus observation becomes more important. The appearance of lips and nail beds tells much about the circulation and gas exchange, whereas presence and quality of peripheral pulses, temperature of the extremities, and capillary refill reveal adequacy of the circulation. Odor provides rough concentration estimates of potent inhalation anesthetics, while observation of external airways, neck, chest, and abdomen gives valuable information about airway patency and adequacy of ventilation. The state of hydration can be assessed by observation of skin turgor, mucous membranes, appearance of external jugular veins, and the eyes. Palpation of the anterior fontanelle of the infant suggests both level of intracranial pressure and hydration.

Breath and heart sounds heard through precordial or esophageal stethoscopes provide much information about the circulation and ventilation. These sounds provide information about cardiac rate, rhythm, and output, blood pressure, adequacy of ventilation, and patency of the airways. Although qualitative in nature and requiring subjective assessment by a trained observer, this information is extremely important, relatively noninvasive, and independent of technology. Using a small radio transmitter, heart and breath sounds can be transmitted to a "Walkman" type receiver worn by the anesthesiologist, giving freedom of movement in the operating room, albeit at the price of dependence on high technology.

Much of this information is lost without access to the patient and must be replaced by other sources of information. These sources generally are more invasive, more dependent on technology, and often carry higher morbidity, so patient access in the operating room should not be surrendered lightly.

The Electrocardiogram

The ECG is valuable in pediatric cardiovascular monitoring for more than heart rate and rhythm. Morphology of QRS, T, and P waves supplies important information concerning both electrolyte levels (K^+ and Ca^{2+}) and the adequacy of myocardial perfusion. Although little appreciated, ST and T wave changes indicative of myocardial ischemia from a number of different etiologies *do* occur in pediatrics and can be important in patient management. Although this occurs most frequently in pediatric cardiac operations, myocardial ischemia may occur whenever the pediatric circulatory system is significantly stressed. A hard copy rhythm ECG strip for later comparison is thus important. As in adult patients, these ischemic or electrolyte ECG changes may not show up in the standard lead II. In major noncardiac operations and virtually all cardiac procedures in children, simultaneous monitoring of two different ECG leads is useful. However, even the use of two simultaneous ECG leads does not ensure that the ECG will show myocardial ischemia or electrolyte abnormalities when present. Esophageal electrocardiography using a no. 12 F esophageal stethoscope equipped with two distal electrodes is useful to analyze supraventricular arrhythmias.[26] The electrodes are connected through an electrocautery protection filter (avoiding esophageal burns) to any standard ECG monitor to give bipolar atrial electrograms. These leads are useful for diagnosing right ventricular ischemia, which may occur relatively frequently in pediatric patients with pulmonary hypertension.[60] Using an external pacemaker, esophageal leads also can be used for transesophageal atrial pacing.[27]

Arterial Blood Pressure Measurement (Noninvasive)

Systemic arterial blood pressure may be measured by using an automated device with a blood pressure cuff, by using a stethoscope and cuff (the traditional Korotkoff technique), with a Doppler flow detector or pulse oximeter and cuff, or with just a cuff alone. The appropriate diameter cuff for extremity size in children is essential for all methods employing cuffs.[36] The automated devices are based predominantly on oscillometric techniques. They have been well validated in children and are quite reliable in most, but not all, circumstances.[21,34] Arrhythmias, hypothermia, and severe hypotension can make these automated devices useless. Any movement impinging on the blood pressure cuff by a surgeon or even from the patient's own chest wall can result in erroneous readings. These are usually signaled by a discrepancy in the indicated heart rate value between the device and the ECG. Sudden very large changes in pressure may not be detected well because inflation pressure of the cuff is based on the previous pressure measurement. Partly on this basis, as well as on others not well described, these automated devices can be inaccurate by as much as 16 to 45 mm Hg.[30] Also, although noninvasive, these automated monitors have been reported to be associated with severe venostasis in an extremity and ulnar nerve palsy when short cycle lengths (1 to 3 minutes) are used for prolonged periods of time.[5,59]

Blood pressure can be measured using a blood pressure cuff with an aneroid sphygmomanometer by employing the rough oscillometric technique variously called the "bounce" or "flicker" technique. After inflation, the cuff is slowly deflated and the indicator needle is watched for oscillations corresponding to the heart beat. The maximum oscillations occur at the mean blood pressure and when measured quantitatively can be very accurate.[68] However, as it is usually measured clinically by eye, the accuracy achieved is probably substantially less. During arrhythmias and periods of severe hypotension, this method is useless. Slow deflation of the cuff, together with palpation of the distal pulse or audible flow signals from a Doppler flow detector fixed over the distal artery, gives good correlations with direct systolic arterial pressure measurements. The Doppler technique is useful during periods of severe hypotension.[35] Alternatively, using a pulse oximeter to detect disappearance of distal flow while *inflating* the cuff can be used in a similar, quite accurate fashion.[37] The deflation technique is less accurate when using a pulse oximeter to detect distal pulses because of a time lag before arterial pulsations are displayed during deflation.[66] This is due to error rejection algorithms in oximeters.

Pulse Oximetry

The pulse oximeter monitors pulsatile delivery of oxygenated blood to the extremities, thus giving effective pulse rates and arterial saturations. Pulse oximetry has been a particular boon to cardiovascular monitoring in children as it allows accurate, on-line assessment of peripheral arterial saturations, allowing certain inferences about the adequacy of the pulmonary as well as the systemic circulation.[48,67] Since most children with congenital heart disease have associated abnormalities in the pulmonary circulation, pulse oximetry thus is particularly valuable. In children, monitoring of the circulation and gas exchange with pulse oximetry now must be considered mandatory in all cases. There are only minimal associated risks so the risk/benefit ratio is so low that there is no excuse for failure to use pulse oximetry in children.[49a] Using pulse oximetry in children, it has been shown that hypoxemia can be diagnosed before potentially damaging cardiovascular effects (bradycardia and hypotension) are apparent.[12]

There are some special situations in pediatrics in which pulse oximetry can be misleading and others in which it is particularly useful. Use of intravenous methylene blue dye, infrared lights, and other intense light sources can give misleading information or otherwise interfere with function of pulse oximeters.[6,11,28] Hypoxemia, however, is well monitored. In cyanotic children and in volunteers, arterial saturations to 40 per cent and below have been accurately measured using transcutaneous pulse oximetry.[39,56] In newborns, the different absorbance of fetal hemoglobin does not appreciably affect the accuracy of pulse oximeters until the concentration of fetal hemoglobin is greater than 50 per cent, in which case the pulse oximeter saturation consistently understates the saturation measured in blood samples by co-oximetry.[31] During transport or in a recovery room where observation and other monitoring is less reliable than in the operating room, pulse oximetry is particularly valuable in children.[17]

In children with intracardiac shunting due to congenital heart disease or an active transitional circulation in neonates, pulse oximetry gives valuable information about pulmonary blood flow when coupled with knowledge of the pathophysiology. In situations in which pulmonary blood flow is critical, that is, weaning from cardiopulmonary bypass or during thoracic procedures in children, the pulse oximeter can be invaluable. Adequacy of pulmonary artery banding can be judged by pulse oximetry in children with congenital heart disease.[9] In neonates with an active transitional circulation, differences in upper and lower extremity saturations are used as an index of right-to-left ductal shunting due to pulmonary artery hypertension. In children with pulmonary disease undergoing major surgery, effects of positioning and surgical manipulations on distribution of pulmonary flow and ventilation in the lung also can be monitored by pulse oximetry.

Transcutaneous Oxygen Monitoring

Transcutaneous oxygen monitoring, because of its hazards, need for calibration, slow response, and long warm-up times, has been completely displaced in pediatric monitoring by pulse oximetry. One possible exception is its use in very premature infants in whom the retinopathy of prematurity makes the measurement of PaO_2 possibly more desirable. However, O_2 tension can no longer be considered the sole environmental stimulus to this form of retinopathy.[42] Nevertheless, maintenance of arterial oxygen saturation in the 95 per cent range measured by pulse oximetry usually assures an arterial PaO_2 of less than 100 mm Hg.

Cardiac Output Monitoring (Noninvasive)

Using pulsed Doppler, continuous wave Doppler, or thoracic impedance measurements, cardiac output in children can be measured noninvasively with varying amounts of accuracy. Continuous wave Doppler measurements of aortic velocity profiles from the sternal notch, combined with an echocardiographic measurement of aortic annulus diameter, have yielded computer-generated cardiac outputs that correlate well with thermodilution outputs in infants and young children after cardiac surgery.[53] However, several minutes are required to position the Doppler probe at the sternal notch for a good image of the aortic flow. This technique thus cannot be considered to be an "on-line" technique and requires access to the sternal notch. Furthermore, in children with right aortic arches or structural abnormalities of left aortic arches, the technique was not accurate. These problems are avoided by continuous wave Doppler probes incorporated into large esophageal stethoscopes used in adults. This technique provides cardiac output values, which in one study correlated well with thermodilution values in adults.[44] However, measurement of aortic diameter and validation with one Doppler measurement from the sternal notch are also required to use the esophageal probe. Currently available probes are too large for use in infants and small children. Pulsed Doppler output techniques provide equally good correlations but also suffer from the need for sternal notch access and manipulation of the probe for optimal flow images.[1,46,50]

Not all investigators have found a good correlation between Doppler output estimation techniques and thermodilution cardiac output.[18] However, because thermodilution itself is invasive and has other shortcomings as a technique, particularly in children, noninvasive Doppler measurements of output may be quite useful, since the measurements are highly reproducible and can accurately detect relative output changes in individual patients.[4,45,55] Doppler techniques also yield reliable estimates of systemic cardiac output in the presence of an intracardiac shunt, whereas indicator dilution methods are invalid when shunts are present.

Changes in thoracic impedance as the result of ejection of blood by the heart also have been used to calculate cardiac output noninvasively. Although commercial devices employing this technique are available that purportedly give accurate on-line cardiac outputs in small children with little attention from the anesthesiologist, these devices have not been adequately validated in clinical use.

INVASIVE MONITORING

Direct Arterial Pressure Monitoring

Direct arterial pressure monitoring using intra-arterial catheters in children yields important beat-to-beat information that is frequently vital to the safe conduct of anesthesia. However, because intra-arterial monitoring in children carries somewhat more risk than in adults, the threshold for use of intra-arterial blood pressure monitoring is thus higher. This is especially true in infants. Cerebral infarcts from a temporal arterial catheter, renal and mesenteric infarction from umbilical artery catheters, or loss of extremity from peripheral arterial catheters have all been reported.[7,52,62] Generally, radial arterial catheters are associated with fewer complications, but in young children radial catheters are not without hazard.[49] One must be cautious about flushing arterial catheters at this or other sites in infants because microbubbles, thrombi, or other particulate matter is forced retrograde into the carotid arteries. This occurs with only a 0.5 ml volume flush in neonatal radial artery lines or with somewhat larger flush volumes in older patients.[8,41]

The choice of a radial artery site must be considered in conjunction with any history of previous or planned aortopulmonary shunts or coarctation repairs that may alter arterial pressures in that arm. Femoral artery catheters are a less desirable alternative, particularly in neonates and small infants in whom the incidence of perfusion-related complications is unacceptably high.[23] A decade ago, major complications with femoral arterial catheters leading to leg amputation were reported in neonates.[69]

In the tiny, reactive arterial vessels of infants, it is particularly important to be aware that peripheral arterial catheters may not accurately reflect central aortic pressure during hypothermia, hypotension, and after weaning from cardiopulmonary bypass.[22,40,58] This is especially true of arterial pressure measurement from foot catheters in infants.[2] If the ascending aorta is readily available, as during cardiac surgery, direct measurement of ascending aortic pressure should be done. In other situations monitoring from other central sites should be performed when the peripheral arterial measurements are suspect. Blood pressure measurements in the upper arm using a cuff frequently will better reflect central pressures than a catheter in more peripheral locations.

Intracardiac Pressure Measurement: General Considerations

Transvenous or transthoracic measurement of atrial and pulmonary arterial pressures provides important physiologic data in the operating room and during the recovery period. Ease of placement and risk of percutaneous central vein catheterization in children differ from that in adults.[57] In infants, threading catheters centrally from peripheral veins is difficult and risks of central approaches to the internal jugular and subclavian veins may be higher, particularly in inexperienced hands. An increased rate of positive catheter tip cultures after percutaneous internal jugular vein catheterization has been reported in infants compared with older children.[14] The low cervical approach to the internal jugular vein, compared with a high cervical approach, has resulted in significant morbidity in children in one report.[13]

In infants and small children without severe heart or pulmonary disease, right- and left-sided atrial pressures are almost identical as ventricular performance is more intimately coupled in the small child. Thus a central venous pressure will be a better indicator of volume status and left-sided filling pressures in the healthy small child. Measurement of pulmonary capillary wedge pressures is thus less frequently required in children.

Pulmonary Artery Catheterization

Pulmonary artery catheterization in the operating room may be difficult or impossible in children and does not always yield clinically useful information, particularly in congenital heart disease, which accounts for the bulk of heart disease in children.[10,57] In children with severe acquired heart disease, indications for pulmonary artery catheterization are similar to those in adults with severe cardiac disease. In sick children with intracardiac congenital defects, percutaneous catheterization of the pulmonary artery using a flow-directed catheter can be very difficult. In these forms of congenital heart disease, left and right atrial or ventricular pressures are often equal because of large septal defects. In these cases a simple central venous catheter adequately reflects left-sided filling pressures as well as right-sided pressures. Many of these patients have pulmonary vascular obstructive disease, making the pulmonary capillary wedge pressure less useful. Owing to intracardiac shunts, thermodilution cardiac output is not reliable. In very small infants and in intracardiac defects such as tricuspid or pulmonary atresia, the transthoracic approach may be the only practical way of inserting pulmonary artery catheters.

When appropriate, right heart and pulmonary catheterization in small children using 5 F balloon-tipped pulmonary artery flotation catheters is feasible, although technically more difficult than with adult-sized 7 F catheters. Relatively little experience with balloon flotation pulmonary artery catheters in children has been reported. In one study of their use in children, a 10 per cent incidence of carotid artery puncture and an 8 per cent incidence of positive catheter tip cultures were noted, along with a 92 per cent incidence of successful placement.[51] These investigators reported that information from the pulmonary artery catheter yielded important diagnostic information in 47 per cent of children and resulted in critical therapeutic interventions in 35 per cent of the children. Pulmonary artery catheters have also been useful in children with cardiomyopathy in a low output state, children in shock following generalized hypoxic-ischemic injury, for estimating intrapulmonary shunt in critically ill children, and for managing pulmonary hypertension in children with acute respiratory failure and in neonates with pulmonary hypertension from various causes.[16,32,43,51]

Other reported experience in children is with transthoracic pulmonary artery catheters inserted at the time of surgery or small, single lumen pulmonary artery catheters inserted under fluoroscopy.[24,63] Transthoracic pulmonary artery catheters have been associated with complications in 1.1 per cent of children. These complications include catheter retention requiring operative removal and intrathoracic bleeding at the time of removal. Bleeding on removal (0.47 per cent) associated with some degree of tamponade and hemodynamic compromise occur most frequently in children with pulmonary hypertension.[24] A small catheter with a single lumen or combined with a thermistor is available for transthoracic use. A separate 2 F pulmonary artery thermistor catheter is also available and, when coupled with a right atrial catheter, is useful for measuring cardiac outputs in small children.[20,54]

Left Atrial Catheters

In children having complex congenital heart operations, left atrial catheters are useful for monitoring left ventricular performance. Monitoring left atrial pressure when weaning from bypass gives useful information about left ventricular performance, circulating volume status, and atrioventricular valve performance. Left atrial catheters must be inserted transthoracically under direct vision. There is a low incidence of bleeding (0.13 per cent) and catheter retention (0.63 per cent) associated with their use.[24] In the presence of pulmonary vascular disease, a reactive pulmonary circulation, or dysfunction of either the left or right ventricle, left atrial catheters are particularly useful because of the limitations of pulmonary artery and right atrial catheters in these situations.

Invasive Cardiac Output Monitoring

Using an arterial withdrawal system or pulmonary artery catheters with thermistors or fiberoptics, an indicator can be injected into the central venous circulation and sampled over time at the pulmonary artery or at a peripheral artery. A cold solution as indicator is used with pulmonary artery thermistor catheters and green dye can be used with fiberoptic pulmonary catheters or peripheral arterial withdrawal. For thermodilution outputs, smaller injectate volumes of 1 to 3 ml can be used in infants and small children with good accuracy.[20,54] However, intracardiac shunts invalidate both these methods. These methods carry a risk of sepsis and are not necessarily any more accurate than Doppler techniques in children.[45,55] Measurements of cardiac output by indicator dilution techniques have been shown to be useful in children after open-heart surgery and other specialized situations.[61] Using miniaturized Doppler flow probes placed on the aorta at the time of surgery and later removed by traction, continuous cardiac output can be accurately and usefully monitored in children following repair of congenital heart disease.[33,64] This technique, although useful, has not become widespread.

Mixed Venous Oxygen Saturation Monitoring

Using pediatric-sized fiberoptic pulmonary artery catheters or withdrawal of samples from pulmonary artery catheters allows monitoring of mixed venous oxygen saturations periodically in the latter technique and moment by moment with the former technique. After repair of intracardiac septal defects, monitoring of mixed venous oxygen can reveal residual left-to-right shunting as evidence of residual septal defects.[38,65] In any patients continuous bedside monitoring of mixed venous oxygen saturation with a fiberoptic pulmonary artery catheter and a bedside processor theoretically indicates the adequacy of the oxygen supply-demand balance of the perfused tissues in the body as a whole. Thus, mixed venous oxygen saturation functions as an early warning of untoward events causing an imbalance of this relationship and provides immediate feedback as to the effectiveness of interventions. Some clinical studies have shown this type of invasive monitoring to be effective in critically ill patients, but there has been no clear demonstration of its value in children.[3] Technical problems with this form of monitoring in small children are somewhat greater than in adults and, outside of a few centers, continuous mixed venmous oxygen saturation monitoring is not widely used.

Two-Dimensional Echocardiography and Color Flow Doppler

Echocardiographic monitoring of cardiac function, color flow Doppler monitoring of the status of intracardiac shunts, and Doppler measurement of flows and pressure gradients are becoming increasingly useful intraoperatively and postoperatively. Although currently, pediatric-size esophageal echocardiogram transducers are not available because of heat production problems, transesophageal echo-Doppler transducers have been used in older children with congenital heart disease to monitor intracardiac shunt flows intraoperatively.[29] Using a transcutaneous transducer when the chest is accessible, or a sterile sheathed transducer applied to the epicardium in an open chest, these measurements can also be done in small infants. If a color Doppler is not available, contrast material such as albumin injected into a central line can be used to visualize intracardiac shunts.[19] Ventricular contractility, valvular function, and cardiac volumes can all be monitored intraoperatively using these techniques, which are currently coming into wider clinical use in pediatrics.[25,47]

APPROPRIATE MONITORING FOR THE PEDIATRIC PATIENT

The great variety of pediatric cardiac and pulmonary disease, the diversity of operative procedures performed in children, and the substantial changes in cardiopulmonary reserve that occur with growth and development even in the normal pediatric cardiopulmonary system all rule out a rigid approach to cardiovascular monitoring in children. Depending on the age, cardiovascular status, proposed operation, and experience and skill of the anesthesiologist, appropriate cardiovascular monitoring in children varies widely. The newer noninvasive monitors now available for children provide more immediate and precise information about the status of both the pulmonary and systemic circulation. This information is particularly useful during the increasingly complex operations done in sick children.

For a general anesthetic in any child undergoing a diagnostic or minimally invasive procedure such as a herniorrhaphy, minimal cardiovascular monitoring equipment consists of a single lead ECG, pulse oximeter, blood pressure cuff, and precordial or esophageal stethoscope. At the other extreme, in an acidotic, hypoxemic newborn with hypoplastic left heart syndrome, the minimal monitoring would be augmented by a second monitored ECG lead such as V_6, a central venous catheter, a radial and perhaps an umbilical artery catheter, pulse oximeters on both an upper and a lower extremity, a pulmonary artery catheter with a thermistor, and a left atrial line inserted during surgery. Additionally, a transcutaneous color Doppler could be used intermittently to monitor intracardiac shunting. Between these two extremes, the mix of monitoring techniques used in children depends on the judgment and skill of the ultimate monitor, the anesthesiologist.

REFERENCES

1. Alverson DC, Eldridge M, Dillon T, et al: Noninvasive pulsed Doppler determinations of cardiac output in neonates and children. J Pediatr 101:46–50, 1982

2. Abou-Madi M, Lenis S, Archer D, et al: Comparison of direct blood pressure measurements at the radial and dorsalis pedis arteries during sodium nitroprusside- and isoflurane-induced hypotension. Anesthesiology 65:692–695, 1986
3. Baele PL, McMichan JC, Marsh HM, et al: Continuous monitoring of mixed venous oxygen saturation in critically ill patients. Anesth Analg 61:513–517, 1982
4. Bernstein DP: Noninvasive cardiac output, Doppler flowmetry, and gold-plated assumptions. Crit Care Med 15:886–888, 1987
5. Betts EK: Hazard of automatic noninvasive BP monitoring. Anesthesiology 55:711–718, 1981
6. Brooks DB, Paulus DA, Winkle WE: Infrared heat lamps interfere with pulse oximeters. Anesthesiology 61:630, 1984
7. Bull MJ, Schreiner RL, Garg BP, et al: Neurologic complications following temporal artery catheterization. J Pediatr 96:1071–1073, 1980
8. Butt WW, Gow R, Whyte H, et al: Complications resulting from use of arterial catheters: Retrograde flow and rapid elevation in blood pressure. Pediatrics 76:250–254, 1985
9. Casthely PA, Redko V, Dluzneski J, et al: Pulse oximetry during pulmonary artery banding. J Cardiothorac Anes 1:297–299, 1987
10. Connors AF, McCaffrey DR, Gray BA: Evaluation of right heart catheterization in critically ill patients without myocardial infarction. N Engl J Med 312:263–267, 1983
11. Costarino AT, et al: Falsely normal saturation reading with the pulse oximeter. Anesthesiology 67:830–831, 1987
12. Coté CJ, Goldstein EA, Coté MA, et al: A single-blind study of pulse oximetry in children. Anesthesiology 68:184–188, 1988
13. Coté CJ, Jobes DR, Schwartz AJ, et al: Two approaches to cannulation of a child's internal jugular vein. Anesthesiology 50:371–373, 1979
14. Damen J: Positive bacterial cultures and related risk factors associated with percutaneous internal jugular vein catheterization in pediatric cardiac patients. Anesthesiology 66:558–562, 1987
15. Damen J, Wever JE: The use of balloon-tipped pulmonary artery catheters in children undergoing cardiac surgery. Intens Care Med 13:266–272, 1987
16. Dean JM, Wetzel RC, Rogers MC: Arterial blood gas derived variables as estimates of intrapulmonary shunt in critically ill children. Crit Care Med 13:1029–1033, 1985
17. DeSoto H, Patel RI, Soliman IE, et al: Changes in oxygen saturation following general anesthesia in children with upper respiratory infection signs and symptoms undergoing otolaryngological procedures. Anesthesiology 68:276–279, 1988
18. Donovan KD, Dobb GJ, Newman MA, et al: Comparison of pulsed Doppler and thermodilution methods for measuring cardiac output in critically ill patients. Crit Care Med 15:853–857, 1987
19. Eguaras MG, Pasalodos J, Gonzalez V, et al: Intraoperative contrast two-dimensional echocardiography. J Thorac Cardiovasc Surg 89:573–579, 1985
20. Freed MD, Keane JF: Cardiac output measured by thermodilution in infants and children. J Pediatr 92:39–42, 1978
21. Friesen RH, Lichtor JL: Indirect measurement of blood pressure in neonates and infants utilizing an automatic noninvasive oscillometric monitor. Anesth Analg 60:742–745, 1981
22. Gallagher JD, Moore RA, McNicholas KW, et al: Comparison of radial and femoral arterial blood pressure in children after cardiopulmonary bypass. J Clin Monitoring 1:168–171, 1985
23. Glenski JA, Beynen FM, Brady J: A prospective evaluation of femoral artery monitoring in pediatric patients. Anesthesiology 66:227–229, 1987
24. Gold JP, Jonas RA, Lang P, et al: Transthoracic intracardiac monitoring lines in pediatric surgical patients: A ten-year experience. Ann Thorac Surg 42:185–191, 1986
25. Goldman ME, Guarino T, Fuster V, et al: The necessity for tricuspid valve repair can be determined intraoperatively by two dimensional echocardiography. J Thorac Cardiovasc Surg 94:542–550, 1987

26. Greeley WJ, Kates RA, Bushman GA, et al: Intraoperative esophageal electrocardiography for dysrhythmia analysis and therapy in pediatric cardiac surgical patients. Anesthesiology 65:669–672, 1986
27. Greeley WJ, Reves JG: Transesophageal pacing for the treatment of dysrhythmias in pediatric surgical patients. Anesthesiology 68:282–285, 1988
28. Hannowell L, Eisele JH, Downs A: Ambient light affects pulse oximeters. Anesthesiology 67:864–865, 1987
29. Hillel Z, Thys D, Ritter S, et al: Two-dimensional color flow Doppler echocardiography for intraoperative monitoring of cardiac shunt flow in patients with congenital heart disease. J Cardiothorac Anesth 1:40–47, 1987
30. Hutton P, Dye J, Prys-Roberts C: An assessment of the Dinamap 845. Anaesthesia 39:261–267, 1984
31. Jennis MS, Peabody JL: Pulse oximetry; an alternative method for the assessment of oxygenation in newborn infants. Pediatrics 79:524–528, 1987
32. Katz R, Pollack MM, Spady D: Cardiopulmonary abnormalities in severe acute respiratory failure. J Pediatr 104:357–364, 1984
33. Keagy BA, Wilcox BR, Lucas CL, et al: Constant postoperative monitoring of cardiac output after correction of congenital heart defects. J Thorac Cardiovasc Surg 93:658–664, 1987
34. Kimble KJ, Darnall RA, Yelderman M, et al: An automated oscillometric technique for estimating mean arterial pressure in critically ill newborns. Anesthesiology 54:423–425, 1981
35. Kirby RR, Kemmerer WT, Morgan JC: Transcutaneous Doppler measurement of blood pressure. Anesthesiology 31:86–89, 1969
36. Kirkendall WM, Burton AC, Epstein FH, et al: Recommendations for human blood pressure determination by sphygmomanometers. Circulation 36:980–988, 1967
37. Korbon GA, Wills MH, D'Lauro F, et al: Systolic blood pressure measurement: Doppler vs pulse oximeter. Anesthesiology 67:A188, 1987
38. Lang P, Chipman CW, Siden M, et al: Early assessment of hemodynamic status after repair of tetralogy of Fallot: A comparison of 24 hour and one year postoperative data in 98 patients. Am J Cardiol 58:795–801, 1980
39. Lazzell VA, Jopling MW: Accuracy of pulse oximetry in cyanotic congenital heart disease. Anesthesiology 67:A169, 1987
40. Lin CY, Beker B, LaFontaine E: Accuracy of radial pressure monitoring [abstract] Anesth Analg 64:247, 1985
41. Lowenstein E, Little JW, Lo HH: Prevention of cerebral embolization from flushing radial artery cannulas. N Engl J Med 285:1414–1415, 1971
42. Lucey JF, Dangman B: A reexamination of the role of oxygen in retrolental fibroplasia. Pediatrics 73:82–96, 1984
43. Lucking SE, Pollack M, Fields AI: Shock following generalized hypoxic-ischemic injury in previously healthy infants and children. J Pediatr 108:359–364, 1986
44. Mark JB, Steinbrook RA, Gugino LD, et al: Continuous noninvasive monitoring of cardiac output with esophageal Doppler ultrasound during cardiac surgery. Anesth Analg 65:1013–1020, 1986
45. Maruschak GF, Potter AM, Schauble JF, et al: Overestimation of pediatric cardiac output by thermal indicator loss. Circulation 65:380–383, 1982
46. Mellander M, Sabel KG, Caidahl K, et al: Doppler determination of cardiac output in infants and children: Comparison with simultaneous thermodilution. Pediatr Cardiol 8:241–246, 1987
47. Meyer RA: Echocardiography—application in assessing cardiac performance in clinical care. Anesthesiology 49:71–78, 1978
48. Mihm FG, Halperin BD: Noninvasive detection of profound arterial desaturation using a pulse oximetry device. Anesthesiology 62:85–87, 1985
49. Miyasaka K, Edmonds JF, Conn AW: Complications of radial artery lines in the paediatric patient. Can Anaesth Soc J 23:9–13, 1976
49a. Miyasaka K, Ohata J: Burn, erosion and "sun" tan with use of pulse oximetry in infants. Anesthesiology 67:1008–1009, 1987

50. Murray D, Vandewalker G, Matherne GP, et al: Pulsed Doppler and two-dimensional echocardiography: Comparison of halothane and isoflurane on cardiac function in infants and small children. Anesthesiology 67:211–217, 1987
51. Peckham GJ, Fox WW: Physiologic factors affecting pulmonary artery pressure in infants with persistent pulmonary hypertension. J Pediatr 93:1005–1010, 1978
52. Prian G, Wright GB, Rumack CM, et al: Apparent cerebral embolization after temporal artery catheterization. J Pediatr 93:115–118, 1978
53. Rein AJJT, Hsieh KS, Elixson M, et al: Cardiac output measurements in the pediatric intensive care unit using a continuous-wave Doppler computer: Validation and limitations of the technique. Am Heart J 112:97–103, 1986
54. Rogers MC, Nugent SK, Pickard LR, et al: Experimental evaluation of 2F transthoracic thermodilution cardiac outputs in small animals. Crit Care Med 7:171–173, 1979
55. Schuster AH, Nanda NC: Doppler echocardiographic measurement of cardiac output: Comparison with a non-golden standard. Am J Cardiol 53:257–259, 1984
56. Severinghaus JW, Naifeh KH: Accuracy of response of six pulse oximeters to profound hypoxia. Anesthesiology 67:551–558, 1987
57. Smith-Wright DL, Green TP, Lock JE, et al: Complications of vascular catheterization in critically ill children. Crit Care Med 12:1015–1017, 1984
58. Stern DH, Gerson JI, Allen FB, et al: Can we trust the direct radial artery pressure immediately following cardiopulmonary bypass. Anesthesiology 62:557–561, 1985
59. Sy WP: Ulnar nerve palsy possibly related to use of automatically cycled blood pressure cuff. Anesth Analg 60:687–688, 1981
60. Trager MA, Fineberg BI, Kaplan JA: Right ventricular ischemia diagnosed by an esophageal electrocardiogram and right atrial pressure tracing. J Cardiothorac Anesth 1:123–125, 1987
61. Truccone NJ, Spotnitz HM, Gersony WM: Cardiac output in infants and children after open-heart surgery. J Thorac Cardiovasc Surg 71:410–414, 1976
62. Tyson JE, deSa DJ, Moore S: Thromboatheromatous complications of arterial catheterization in the newborn period. Arch Dis Child 51:744–754, 1976
63. Vacanti JP, Crone RK, Murphy JP, et al: The pulmonary hemodynamic response to perioperative anesthesia in the treatment of high-risk infants with congenital diaphragmatic hernia. J Pediatr Surg 19:672–679, 1984
64. Van Orden DE, Farley DB, Fastenow C, et al: A technique for monitoring blood flow changes with miniaturized Doppler flow probes. Am J Physiol 247:H1005–1009, 1984
65. Vincent RN, Lang P, Chipman C, et al: Assessment of hemodynamic status in the intensive care unit immediately after closure of ventricular septal defects. Am J Cardiol 55:526–531, 1985
66. Wallace CT, Baker JD, Alpert CC, et al: Comparison of blood pressure measurement by Doppler and by pulse oximetry techniques. Anesth Analg 66:1018–1019, 1987
67. Yelderman M, New W: Evaluation of pulse oximetry. Anesthesiology 59:349–352, 1983
68. Yelderman M, Ream AK: Indirect measurement of mean blood pressure in the anesthetized patient. Anesthesiology 50:253–256, 1979
69. Zerella JT, Trump DS, Dorman GW: Access for neonatal arterial monitoring. J Pediatr Surg 14:270–275, 1979

Department of Anesthesia
The Children's Hospital
300 Longwood Avenue
Boston, MA 02115

0889-8537/88 $0.00 + .20

Monitoring the Coronary Circulation

Richard I. Hall, MD, FRCP(C), and*
Emerson A. Moffitt, MD, FRCP(C)†

To understand the techniques employed to monitor changes in the coronary circulation induced by anesthesia and surgery, it is necessary to have an appreciation of the anatomy and physiology of this unique circulation. Against this background we will review the current methods employed to monitor changes in coronary blood flow and myocardial metabolism and their relevance to anesthesia.

ANATOMY OF THE CORONARY CIRCULATION

Arterial Blood Supply

The arterial supply to the myocardium is via the right and left coronary arteries[42] that have their origin from the respective cusp regions of the aortic root.

The left coronary artery passes behind the pulmonary trunk to emerge on the left side of the heart where within a short distance it divides into two or more major arteries: the left anterior descending (LAD), the circumflex (Cx), and occasionally a diagonal artery. The LAD passes in the anterior interventricular septum to terminate around the apex, giving rise to diagonal and septal perforating branches. The LAD and its branches supply blood to most of the ventricular septum, to the anterior, lateral, and apical wall of the left ventricle and to the anterolateral papillary muscle of the left ventricle. The circumflex artery runs posteriorly around the left side of the heart in the left atrioventricular (AV) sulcus and in 10 to 15 per cent of patients continues to form the posterior descending artery (PDA) on the posterior surface of the heart. It supplies the left atrial wall, posterior and lateral left ventricle, anterolateral papillary muscle and, in 40 to 50 per cent of patients, the sinus node artery.

The right coronary artery runs in the posterior AV groove to ter-

---

Dalhousie University and The Victoria General Hospital, Halifax, Nova Scotia, Canada

*Assistant Professor of Anaesthesia and Pharmacology
†Professor, Department of Anaesthesia

Supported in part by a grant from the Nova Scotia Heart Foundation

minate as a left ventricular branch. Its divisions include the conus artery to the right ventricular outflow area, the sinus node artery (40 to 50 per cent of patients), the AV node artery, and the PDA (90 per cent of patients). The right coronary artery supplies blood to the sinus node, right ventricular wall, crista supraventricularis, and the right atrium. The PDA supplies the basilar posterior ventricular septum, AV node, proximal His bundle, half the diaphragmatic surface, and the posteromedial papillary muscle of the left ventricle.

In man, the left coronary artery supplies the dominant portion of circulation to the ventricles in 20 per cent of patients, both right and left arteries in 30 per cent, and the right coronary artery in the remaining 50 per cent.[4] There is also an extensive collateral network capable of providing flow between epicardial vessels and at the endocardial level.[12]

Venous Drainage

The venous drainage of the heart is composed of three different systems. The coronary sinus system receives blood from the great, middle, and small cardiac veins, the posterior veins of the left ventricle, and the left atrial oblique vein. The coronary sinus drains 96 per cent of the veins of the left ventricle.[23] However, 17 per cent of coronary sinus blood flow is composed of venous drainage from other than the left ventricle. Of this 17 per cent, a large proportion enters via the posterior cardiac vein, draining the posterior aspect of the heart (right-sided circulation). Studies measuring blood flow in the coronary sinus and extrapolating the results as indicative of changes in left-sided blood flow must be interpreted within the context of this anatomy. Hence the proper placement of coronary sinus catheters within the coronary sinus is important.[3,33,43]

The second venous drainage system involves the anterior cardiac veins, which drain directly into the right atrium.[23] The third venous drainage system comprises thebesian vessels that drain directly into the cardiac chambers, primarily the right atrium and ventricle.[23] Gregg and Shipley[16] have demonstrated that an extensive collateral network exists for the venous drainage of the heart.

PHYSIOLOGY OF THE CORONARY CIRCULATION

Metabolic Control

Control of the coronary circulation occurs foremost at the cellular level. In healthy patients the blood flow to the myocardium is approximately 70 ml $\cdot$ min^{-1} $\cdot$ 100 g^{-1}.[26] The heart has only limited ability to function under anaerobic conditions and a continuous supply of well-oxygenated blood is essential for normal myocardial function.[25,29,36,41] The myocardium normally extracts approximately 70 per cent of the oxygen supplied to it. Hence increasing demand for oxygen from increased metabolic need is met by increasing blood flow with little change in coronary sinus mixed venous oxygen content even under conditions of severe exercise.[45] Blood flow to the myocardium is therefore largely dependent on metabolic need.[34]

The heart is capable of utilizing a variety of substrates for energy production via the Krebs cycle including glucose, free fatty acids, lactate, and pyruvate. Fatty acids are utilized in preference to other substrates when available. Under aerobic conditions 20 to 30 per cent of arterial lactate is extracted and metabolized and lactate is not normally produced by the myocardial cell.[15,27,41] Cellular levels of high-energy compounds such as ATP and creatine phosphate and their breakdown products (ADP, AMP, and inorganic phosphate) serve to regulate metabolism at the cellular level. Various substances have been implicated as blood flow regulators in response to metabolic needs and include carbon dioxide, reduced levels of cellular oxygen, lactic acid, hydrogen ions, histamine, potassium ions, increased osmolarity, polypeptides, prostaglandins, and adenine nucleotides. The latter are currently favored as the metabolic vasodilator.[4,37,38]

The coronary arteries have the ability to constrict or dilate in the presence of changing coronary perfusion pressures so as to maintain a relatively constant supply of blood to the coronary tissues in the face of a constant oxygen demand (myogenic or autoregulation).[25,37] In a review of the effects of volatile anesthetic agents on the microcirculation, Longnecker[30] concluded that halothane and enflurane appear to leave coronary artery autoregulatory mechanisms intact. Isoflurane produces a "luxury perfusion" with increased coronary perfusion due to coronary artery dilatation occurring even in the presence of reduced myocardial oxygen demand.[30] More recently Hickey et al, in a study of the effects of volatile anesthetic agents on coronary autoregulation in dogs, concluded that 1.0 MAC of halothane, enflurane, and isoflurane mildly disrupted autoregulation. Isoflurane produced the greatest change. None of the agents could be considered a powerful coronary artery vasodilator and indeed the maximal coronary artery blood flow and coronary vascular reserve (see following) were unchanged from the awake state.[20]

When blood flow fails to meet tissue demands for oxygen, anaerobic metabolism ensues, with production of metabolites including an excess of intracellular lactate, which can be measured in the venous effluent from the ischemic area. Contractility is rapidly impaired.[41]

Mechanical Factors

Coronary blood flow is dependent on the maintenance of an adequate aortic perfusing pressure and changes in coronary vascular resistance.[11] This can be represented as

$$\dot{Q} = P/R$$

where $\dot{Q}$ represents coronary blood flow, P = aortic perfusing pressure, and R = coronary vascular resistance. This concept ignores the influence of inertia (blood velocity) and elastic components (blood vessel wall elasticity), which may play roles in overall impedance to blood flow, but these changes are felt to be of minor importance.[25] The resistance to coronary blood flow can be considered under three separate components: (1) that due to basal viscous resistance, which is present when the coronary bed is fully dilated in diastole; (2) autoregulatory resistance due to changes in metabolic need; and (3) that due to compressive resistance from contraction of the myocardial cells during the cardiac cycle. The latter component is substantial and exerts most of its influence during systole.[9,31] There is also a transmural pressure gradient with the endocardium affected more than the epicardium.[6,8,22] Blood flow in a large coronary artery supplying the left ventricle may be transiently reversed during systole.[4,8,43] Maximal coronary inflow occurs during diastole. Blood flow to all areas of the myocardium is equal during diastole in spite of the transmural pressure gradient.[5] This suggests that the vasodilatory reserve of the endocardium in response to increased myocardial energy requirements (the coronary reserve[21]), is relatively impaired compared with that of the epicardium. This may be one explanation for the relative susceptibility of the endocardium to ischemic insults especially when diastolic perfusing time is limited (for example, tachycardia).[2,5,22]

In patients with coronary artery disease, flow across the stenosis is impaired and resistance is increased. Increasing flow across the stenosis further increases the resistance and exacerbates the pressure fall across the stenosis, thereby impairing flow beyond the stenosis.[11] Owing to the reduced flow distal to the obstructing lesion, coronary reserve may be maximally utilized. Vasodilator drugs that increase flow in epicardial vessels rather than to the ischemic endocardium may exacerbate the problem and precipitate further ischemia ("coronary steal").[11,13,17]

Neural Factors

While the primary factor regulating local myocardial perfusion is metabolic, some neural influence is also present. Stimulation of the vagal nerves to the heart has little effect on coronary arteriolar diameter although intracoronary injection of cholinergic agents elicits marked vasodilatation.[4] The coronary vessels possess alpha- (constrictor) and beta- (dilator) adrenergic receptors. Studies in dogs suggest that stimulation of the alpha receptors modulates the coronary artery vasodilation in response to exercise,[35] even in the presence of coronary stenosis.[7] Poststenotic vessels that are maximally dilated to compensate for stenosis may remain susceptible to adrenergic vasoconstriction with the production of ischemia in the region distal to the stenosis.[19]

Humoral Influences

Coronary vessels are lined with endothelial cells capable of altering blood flow through interactions with circulating blood elements, with the subsequent release of vasoactive substances.[10]

Through an interaction between the endothelium, prostaglandins, and circulating blood elements (particularly platelets) various mediators have been implicated as responsible for changes in coronary blood flow.[18] These substances include serotonin (vasodilation), adenine nucleotides (vasodilation), and platelet-activating factor (vasoconstriction). The exact role each of these substances plays in the normal regulation of coronary arterial tone remains to be elucidated.

METHODS OF MONITORING THE CORONARY CIRCULATION

Inert Gas Washout Technique

This method for measuring coronary artery blood flow depends on the measurement of the arteriovenous concentration difference of an inert gas, for example, xenon, nitrous oxide, krypton, or helium, over time and solving the equation

$$\text{Flow/unit wt} = 100 \times \lambda \cdot \Delta C_v / {}_0\int^t (C_a - C_v)dt$$

where λ is the tissue-blood partition coefficient for the indicator gas, C_v is the coronary venous blood concentration (from the coronary sinus) and C_a is the arterial concentration.[25] The method has several deficiencies including inability to sample flow directly from the area of the myocardium of interest (for example, region of perfusion of the LAD) and the relative underrepresentation of areas with low perfusion unless sufficient time is allowed to permit tissue equilibrium to occur (at least 10 to 20 minutes for most gases). The method also suffers from problems with recirculating tracer gases during the observation period and solubility of the tracer gases in cardiac adipose tissue, leading to false values for flow when compared with that measured directly with electromagnetic flow probes. These deficiencies have prevented effective application of the technology to anesthetic research.

Coronary Sinus Flow Catheter

In 1971, following their experience with measuring cardiac output via a thermodilution technique with a specialized catheter, Ganz et al introduced the coronary sinus thermodilution catheter (Figs. 1 to 3).[14] With the catheter, flow in the coronary sinus could be measured along with sampling of blood for a variety of substances including lactate and coronary sinus mixed oxygen content.[14] The flow measurement was based on the following formula:

$$\text{CSBF} = F_I \times 1.08 \times (T_B - T_I/T_B - T_M - 1)$$

where F_I is the infusion rate of the indicator, 1.08 is a factor based on the densities and specific heat of blood and indicator when normal

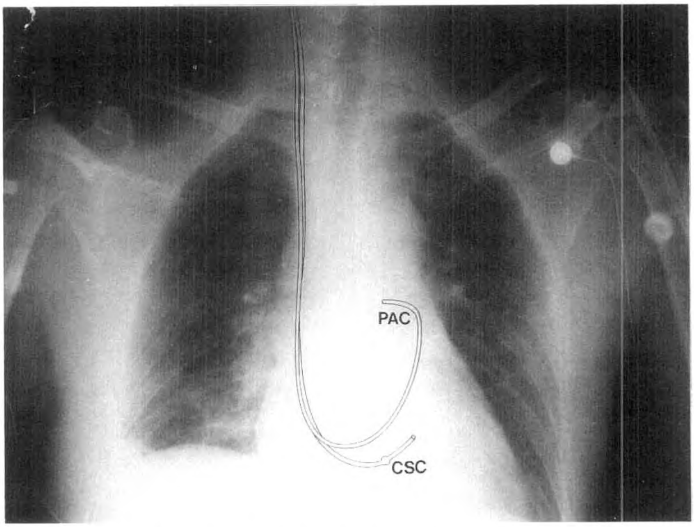


Figure 1. Chest radiograph showing the coronary sinus catheter in situ with its typical caudad relationship to the pulmonary arterial catheter. PAC = pulmonary artery catheter, CSC = coronary sinus catheter.

saline or 5 per cent dextrose is used, and T_B, T_I, and T_M are the temperatures (°C) of the blood, indicator, and mixture, respectively.

In dogs, in which total coronary sinus blood flow was measured directly by blood collection and with the thermodilution technique, a correlation was noted ($r = 0.987$). In humans the measurement was reproducible (±4 per cent) provided the injection rate was greater than 35 ml per minute. Problems with measurement of recirculating indicator were not encountered as the body is a large heat sink. The calculated flow per unit weight of myocardium was similar to that calculated using the inert gas washout technique. Ganz and colleagues concluded that the technique was safe, reproducible, simple to employ, and useful in situations in which it was necessary to measure rapid changes in coronary blood flow. Disadvantages of the

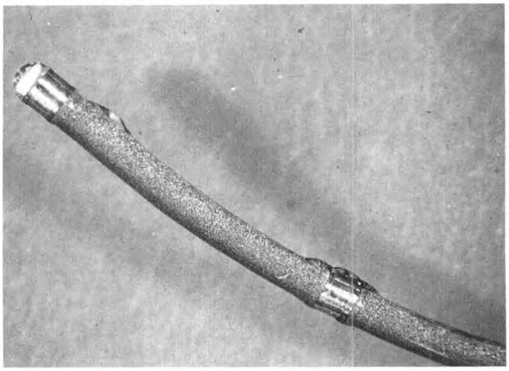


Figure 2. Catheter tip of the Ganz coronary sinus catheter, with its side injection and sample withdrawal port. The external thermistor is downstream from the ejection port; the internal one within the lumen.

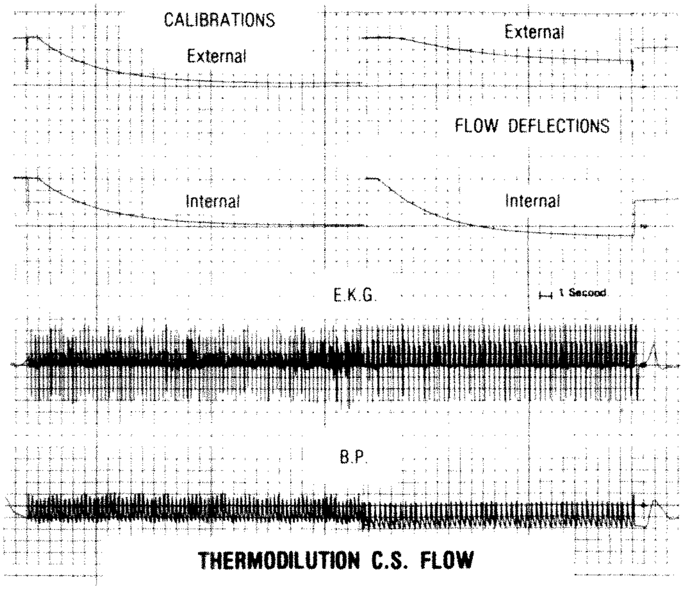


Figure 3. Typical coronary sinus thermodilution flow measurement. Infusate at 40 ml per minute over about 20 seconds gives internal thermistor deflection. External deflection is inverse to the rate of total coronary sinus blood flow.

method were that it required catheterization of the coronary sinus and withdrawal of blood for sampling was slower and at times more difficult, than with the inert gas technique. Also with repeated measurements, relatively large volumes of solution were injected.

During cardiopulmonary bypass in dogs, VanDevanter et al compared flow measured by electromagnetic flow meter with that measured by the coronary sinus catheter; their correlation was $r = 0.90$.[46] However, Mathey et al[32] were able to demonstrate that coronary sinus reflux of right atrial blood could significantly increase the measured value for flow unless the catheter was advanced well into the coronary sinus. Weisse and Regan[48] compared thermodilution coronary sinus blood flow with that obtained utilizing krypton. In their study only 60 per cent of total LV blood flow was determined by the coronary sinus catheter. They attributed the discrepancy to changes in the position of the catheter within the coronary sinus, due to movement from myocardial contraction and catheter softening. They pointed out that these methodological problems would occur in humans, but perhaps to a lesser degree since the coronary sinus in humans is larger (9 to 12 versus 6 to 7.5 cm). Also in humans right ventricular venous inflow into the sinus occurs near the distal 2 to 3 cm of the sinus near the right atrial opening. Other potential but uninvestigated sources of error in measurement include arrhythmias, changes in intrapleural pressure, and the use of vasodilators that could alter the temperature of coronary sinus blood.[43] It was these considerations that led Baim et al to redesign the catheter (Fig. 4), adding the capability to measure

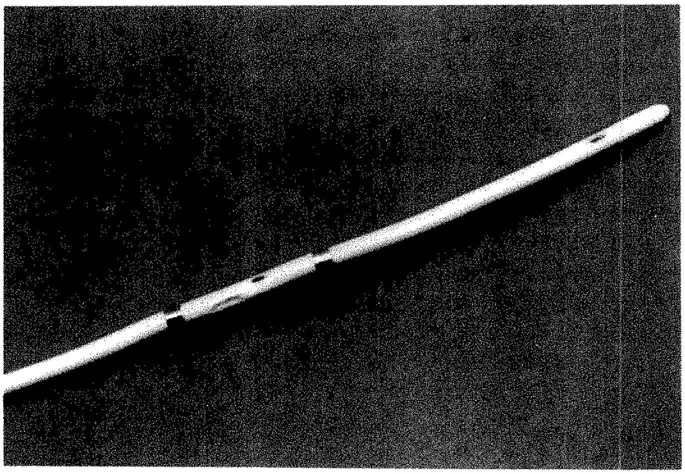


Figure 4. Catheter tip of the Baim coronary sinus catheter. Catheter tip with injecting/sampling port measures great cardiac vein flow.

flow in the great cardiac vein. This vein drains flow from the left ventricle and is the largest branch draining into the coronary sinus, contributing approximately a third of the total coronary sinus flow.[3] This latter catheter is now used in many studies from cardiological laboratories utilizing thermodilution to measure total coronary sinus and great cardiac vein flow.

In addition to measuring coronary blood flow, the catheter is used to sample blood from the coronary sinus for any blood-borne substance including venous oxygen content (abnormally decreased when coronary arterial inflow is unable to supply sufficient oxygen to meet myocardial demand), lactate ion (normally extracted from coronary blood and present only with anaerobic metabolism and ischemia),[15,27] potassium, inorganic phosphate, and hydrogen ion (present in increased concentrations with ischemia).[38,39] Apstein et al,[1] utilizing isolated rat and rabbit hearts, showed that while the presence of lactate in coronary sinus blood was indicative of ischemia, it reflected neither the magnitude nor the duration of the ischemia. Finally, it must be appreciated that detection of markers for ischemia (for example, lactate ion) in coronary sinus outflow (which is the aggregate global flow from the ventricle) may fail to detect small amounts of these substances produced in a local area of ischemia in left ventricular muscle.

Despite these recognized deficiencies, the coronary sinus catheter has been useful for examining the effects of drugs employed during anesthesia and surgery for patients with coronary artery disease. In a series of experiments recently reviewed by Moffitt and Sethna,[33] utility of the catheter has been demonstrated for determining (1) that cardiac medications should be continued prior to cardiac operations, (2) the need for heavy premedication to avoid hypertension and ischemia with its potentially adverse outcome,[44] (3) the value of opiates in combination with volatile agents in preventing hemodynamic response to surgical stimulation, (4) the potential detrimental effect of nitrous oxide in the production of myocardial ischemia, and (5) the production of ischemia, possibly by coronary steal, by high concentrations of isoflurane (independently verified by other groups utilizing different protocols[29,40]). The catheter has also been useful for measuring the sensitivity of other monitors in detecting myocardial ischemia (for example, ECG) and provided support for the widespread use of nitroglycerin by cardiac anesthesiologists to reduce myocardial filling pressures and hence cardiac work. That inotropes can be effective in patients with early ventricular failure, without upsetting myocardial oxygen balance, has also been demonstrated.

Isotopes and Cardiac Imaging Techniques

Radioisotopes are utilized to provide information about myocardial ischemia or infarction.[47] Two general classes are available, those assimilated into ischemic or infarcted tissues and those taken up by normal myocardium. As an example of the first group, technetium 99 is taken up by ischemic tissue and becomes positive within 12 to 14 hours after the onset of myocardial infarction and returns to normal within 1 week. Its utility in the anesthetic situation is limited by the requirement that 12 hours must elapse prior to a positive scan.

In the second class, an isotope is deposited in normal myocardium, leaving infarcted tissue as a "cold spot" on the scan. Underperfused areas are detected by a gradual reduction in the filling defect observed in the initial scan. Examples of these isotopes include potassium 43, rubidium 81, cesium 129, and thallium 201. In a novel application of this technology to anesthesia, Kleinmann and coworkers performed preoperative thallium scans on 22 patients scheduled for coronary artery bypass grafting, then repeated the scan following intubation and postoperatively.[24] Ten patients developed new perfusion defects following intubation even though there were no other hemodynamic changes suggestive of ischemia.

This method, however, has several drawbacks. It is necessary to expose patients to a radioisotope with specialized equipment and facilities, plus the technical expertise required in the handling of radioisotopes. Furthermore, only discrete events can be monitored during the operative procedure; that is, utility of the method during anesthesia and operation must be questioned. Sensitivity of the method for picking up small areas of ischemia developing during anesthesia is as yet unknown; that is, no satisfactory method is available to quantitate the magnitude of ischemia other than its presence or absence.

SUMMARY

Current methods for monitoring the coronary circulation employ two techniques: (1) measurement of coronary sinus blood flow and content of substances known to be altered (for example, venous oxygen content) or produced (for example, lactate ion) during episodes of myocardial ischemia, or (2) use of radioisotopes to measure changes in coronary perfusion to areas of the myocardium at risk for ischemia.

The first method, employing the coronary sinus thermodilution catheter, suffers from a lack of specificity for blood flow in regions of myocardium, but is sensitive for ischemia of sufficient global magnitude to cause changes in coronary sinus content of the measured variables. Data provided by this monitor are retrospective in nature, since the intraoperative assay of substances such as lactate ion is not widely available. Nevertheless, the information has been useful in determining which anesthetic drugs and combinations have the potential to exacerbate or avoid ischemia in patients at risk. Its future use will likely be directed at the further investigation of effects of various anesthetic agents and surgical interventions on the production of myocardial ischemia and as a tool to compare the sensitivity of other monitors for the detection of myocardial ischemia.

Radioisotope flow scanning is both sensitive and specific for the presence of myocardial ischemia, but complex requirements for the use of a radioactive isotope restrict its general applicability.

REFERENCES

1. Apstein CS, Gravino F, Hood WB: Limitations of lactate production as an index of myocardial ischemia. Circulation 60:877–888, 1979
2. Bache RJ, Cobb FR: Effect of maximal coronary vasodilation on transmural myocardial perfusion during tachycardia in the awake dog. Circ Res 41:648–653, 1977
3. Baim DS, Rothman MT, Harrison DC: Improved catheter for regional coronary sinus flow and metabolic studies. Am J Cardiol 46:997–1000, 1980
4. Berne RL, Levy MN: Cardiovascular Physiology, ed. 4. St. Louis, C.V. Mosby, 1981, pp 211–222
5. Boatwright RB, Downey HF, Bashour FA, et al: Transmural variation in autoregulation of coronary blood flow in hyperperfused canine myocardium. Circ Res 47:599–609, 1980
6. Brandi G, McGregor M: Intramural pressure in the left ventricle of the dog. Cardiovasc Res 3:472–475, 1969
7. Buffington CW, Feigl EO: Adrenergic coronary vasoconstriction in the presence of coronary stenosis in the dog. Circ Res 48:416–423, 1981
8. Chilian WM, Marcus ML: Phasic coronary blood flow velocity in intramural and epicardial coronary arteries. Circ Res 50:775–781, 1982
9. Downey JM, Downey HF, Kirk ES: Effects of myocardial strains on coronary blood flow. Circ Res 34:286–292, 1974
10. Dusting DJ: Coronary vasomotor tone: The role of prostanoids re-examined. Bibl Cardiol 38:178–188, 1984
11. Epstein SE, Cannon RO III, Talbot TL: Hemodynamic principles in the control of coronary blood flow. Am J Cardiol 56:4E–10E, 1985
12. Estes EH, Entman ML, Dixon HB II, et al: The vascular supply of the left ventricular wall. Am Heart J 71:58–67, 1966
13. Fam WM, McGregor M: Effect of coronary vasodilator drugs on retrograde flow in areas of chronic myocardial ischemia. Circ Res 15:355–365, 1964
14. Ganz W, Tamura K, Marcus HS, et al: Measurement of coronary sinus blood flow by continuous thermodilution in man. Circulation 44:181–195, 1971

15. Gertz EW, Wisneski JA, Neese R, et al: Myocardial lactate metabolism: Evidence of lactate release during net chemical extraction in man. Circulation 6:1273–1279, 1981
16. Gregg DE, Shipley RE: Studies of the venous drainage of the heart. Am J Physiol 151:13–21, 1947
17. Goldstein RE: Coronary vascular responses to vasodilator drugs. Prog Cardiovasc Dis 24:419–436, 1982
18. Harrison LR, Levin RI: Implications of the dynamic aspects of coronary arterial function for understanding myocardial ischemia. Prob Anesth 1:378–393, 1987
19. Heusch G, Deussen A, Schipke J, et al: Cardiac sympathetic nerve activity and progressive vasoconstriction distal to coronary stenosis: Feed-back aggravation of myocardial ischemia. J Auton Nerv Syst 13:311–326, 1985
20. Hickey RF, Sybert PE, Verrier ED, et al: Effects of halothane, enflurane, and isoflurane on coronary blood flow autoregulation and coronary vascular reserve in the canine heart. Anesthesiology 68:21–30, 1988
21. Hoffman JIE: Maximal coronary flow and the concept of coronary vascular reserve. Circulation 70:153–159, 1984
22. Hoffman JIE: Transmural myocardial perfusion. Prog Cardiovasc Dis 24:429–464, 1987
23. Hood WB: Regional venous drainage of the human heart. Br Heart J 30:105–109, 1968
24. Kleinman B, Henkin RE, Glisson SN, et al: Qualitative evaluation of coronary flow during anesthetic induction using thallium-201 perfusion scans. Anesthesiology 64:157–164, 1986
25. Klocke FJ: Coronary blood flow in man. Prog Cardiovasc Dis 24:117–166, 1976
26. Klocke FJ, Bunnell IL, Greene DG, et al: Average coronary blood flow per unit weight of left ventricle in patients with and without coronary artery disease. Circulation 50:547–559, 1974
27. Kugler G: Myocardial release of lactate, inosine and hypoxanthine during atrial pacing and exercise-induced angina. Circulation 59:43–49, 1979
28. Larsen R, Hilfiker O, Merkel G, et al: Myocardial oxygen balance during enflurane and isoflurane anesthesia for coronary artery disease [abstract]. Anesthesiology 61:A4, 1984
29. Liedtke AJ: Alterations of carbohydrate and lipid metabolism in the acutely ischemic heart. Prog Cardiovasc Dis 23:321–336, 1981
30. Longnecker GE: Effects of general anesthetics on the microcirculation. Microcirc Endo Lymph 1:129–150, 1984
31. Marzilli M, Goldstein S, Sabbah HN, et al: Modulating effect of regional myocardial performance on local myocardial perfusion in the dog. Circ Res 45:634–641, 1979
32. Mathey DG, Chatterjee K, Tyberg JV, et al: Coronary sinus reflux—a source of error in the measurement of thermodilution coronary sinus flow. Circulation 57:778–786, 1978
33. Moffitt EA, Sethna DH: The coronary circulation and myocardial oxygenation in coronary artery disease: Effects of anesthesia. Anesth Analg 65:395–410, 1986
34. Mosher P, Ross J Jr, McFate PA, et al: Control of coronary blood flow by an autoregulatory mechanism. Circ Res 24:250–259, 1964
35. Murray PA, Vatner SF: Alpha-adrenergic attenuation of the coronary vascular response to severe exercise in the conscious dog. Circ Res 45:654–660, 1979
36. Neely JR, Morgan HE: Relationship between carbohydrate and lipid metabolism and the energy balance of heart muscle. Ann Rev Physiol 36:413–459, 1974
37. Nuutinen EM: Regulation of coronary blood flow. Ann Chir Gynaecol 76:12–21, 1987
38. Olsson RA, Bunger R: Metabolic control of coronary blood flow. Prog Cardiovasc Dis 24:369–387, 1987
39. Opie LH, Owen P, Thomas M, et al: Coronary sinus lactate measurements in assessment of myocardial ischemia. Am J Cardiol 32:295–305, 1973
40. Reiz S, Balfours E, Sorenson MB, et al: Isoflurane—a powerful coronary vasodilator in patients with coronary disease. Anesthesiology 59:91–97, 1983

41. Scheuer J: Myocardial metabolism in cardiac hypoxia. Am J Cardiol 19:385–392, 1967
42. Schlant RC, Silverman ME: Anatomy of the heart. *In* Hurst WJ (ed): The Heart Arteries and Veins, ed 6. Toronto, McGraw-Hill, 1986, pp 16–36
43. Sethna DH, Moffitt EA: An appreciation of the coronary circulation. Anesth Analg 65:295–305, 1986
44. Slogoff S, Keats AS: Does perioperative myocardial ischemia lead to postoperative myocardial infarction? Anesthesiology 62:107–114, 1985
45. Stone HL: Control of the coronary circulation during exercise. Ann Rev Physiol 45:213–227, 1983
46. VanDevanter SH, Mills RM Jr, Lesch M, et al: Thermodilution measurement of coronary sinus blood flow during cardiopulmonary bypass. Surg Forum 26:225–227, 1975
47. Waters DD, Forrester JS: Myocardial ischemia: Detection and quantitation. Ann Intern Med 88:239–250, 1978
48. Weisse AB, Regan TJ: A comparison of thermodilution coronary sinus blood flows and krypton myocardial blood flows in the intact dog. Cardiovasc Res 8:526–533, 1974

Dalhousie University and The Victoria General Hospital
Room 10-031
1278 Tower Road
Halifax, Nova Scotia
Canada B3H 2Y9

Monitoring Right Ventricular Function

*Roberta Hines, MD**

An increased awareness of the importance of right ventricular (RV) function in governing overall myocardial performance has recently developed.[29] As a result, more attention has now become focused on employing techniques aimed at monitoring RV function.[37] Of particular interest to the anesthesiologist is the ability to diagnosis RV ischemia/infarction during the perioperative period.[27b,30]

Anatomically, the right ventricle is defined by an inferior and an anterolateral wall. The inferior wall is supplied by the posterior descending branch of the right coronary artery. The anterolateral wall is perfused by the acute marginal branch (from the left coronary artery), the conus branch (from the right coronary artery), and moderator branch of the left anterior descending artery.[1] This highly developed collateral circulation has been cited as one possible factor for the low incidence of reported clinically significant RV infarctions.[26] However, in patients with RV hypertrophy, an accompanying increase in myocardial oxygen demand may place these patients at an increased risk for development of RV infarction.[54]

The clinical recognition of RV ischemia/infarction has only recently received attention, although the characteristics of RV infarction were described by pathologists nearly 50 years ago.[34] This delay in recognition may be due to the fact that earlier electrocardiologists believed that RV necrosis was an electrically silent event (secondary to smaller electrical potential generated by the RV). However, following the first description of the "syndrome of right ventricular dysfunction in the setting of acute inferior wall myocardial infarction" by Cohn et al, numerous studies have documented the ability to diagnose RV ischemia/infarction using the surface electrocardiogram.[13,14]

Standard monitoring for left ventricular ischemia/infarction uses lead V_5 in combination with lead II.[8] However, as a result of the location and geometry of the right ventricle, this lead configuration provides a very limited view of the right ventricle and is often unable to detect early signs of right ventricular dysfunction.[44] New lead

---

*Assistant Professor of Anesthesiology, Director, Cardiothoracic Intensive Care Unit, Department of Anesthesiology, Yale University School of Medicine, Yale-New Haven Hospital, New Haven, Connecticut placement systems now allow for a more specific electrocardiographic image of the RV. Klein et al have determined the sensitivity and specificity of using the V_4R lead.[33] Using radionuclide studies and echocardiography to verify the presence of RV dysfunction seen by EKG, they found that the V_4R lead is a highly specific means of detecting RV ischemia. In 1985, Wellens reported that exercise induced ST-segment elevation or depression of 1 mm or greater in lead V_4R during a treadmill stress test can be used as an accurate predictor of proximal right coronary artery stenosis.[56] As a result of these studies, it appears that the V_4R lead offers a sensitive as well as specific, electrocardiographic means to detect RV ischemia.

Erhardt et al recorded ST-segment elevation (of more than 1 mm) in the CR_4R lead (fifth intercostal space at the right midclavicular line) in ten patients (10/17) with autopsy-proven, fresh, right ventricular infarcts.[19] Subsequently, Chou et al reported transient ST-segment elevation in the precordial lead V_1 in eight patients (8/11) presenting with acute myocardial infarction. The diagnosis of right ventricular infarction was documented by autopsy in five of these patients and by hemodynamic monitoring in six.[13] Additionally, RV infarction may also be associated with ST elevation in the conventional precordial leads (leads V_2 to V_5) and as a result may mimic an anterior myocardial infarction. Croft et al also found elevation of the ST segment in at least one right precordial lead in 11 consecutive patients (11/33) with an acute inferior wall myocardial infarction.[16] Virmani et al have reported a case of isolated RV infarction associated with ST-segment elevation in leads V_1 to V_5.[53] At autopsy, the patient had an isolated RV infarction without any evidence of left ventricular necrosis. The authors postulated that these ST-segment elevations (in the precordial leads) are the result of RV dilatation with a subsequent clockwise rotation of the myocardium. Of note, in this case of RV infarction the degree of ST-segment elevation in the precordial leads (V_1 to V_5) decreases from right to left, with the maximal ST-segment elevation present in lead V_1. Thus, it appears that ST-segment changes in either CR_4R, V_1, or V_4R, are highly specific for identifying patients who are at an increased risk for the development of right ventricular ischemia (Fig. 1).[13,16,19,23,53] As an adjuvant diagnostic modality, Trager et al have recently documented the ability of the esophageal electrocardiogram to diagnose RV ischemia.[50] They demonstrated that this is a valuable addition for the specific and sensitive detection of RV ischemia, particularly in patients with right coronary artery lesions.

In addition to electrocardiography, comprehensive evaluation of RV performance should include the determination of pressure and volume measurements. Normal RV pressure is approximately 25/0-6 mm Hg. Traditionally, central venous pressure measurements (right atrial pressure) have been used as an indicator of RV pressures and volume changes. However, depending on the compliance changes of the RV, and/or abnormalities in the tricuspid valve apparatus, central venous pressure may be an inadequate predictor of right ventricular

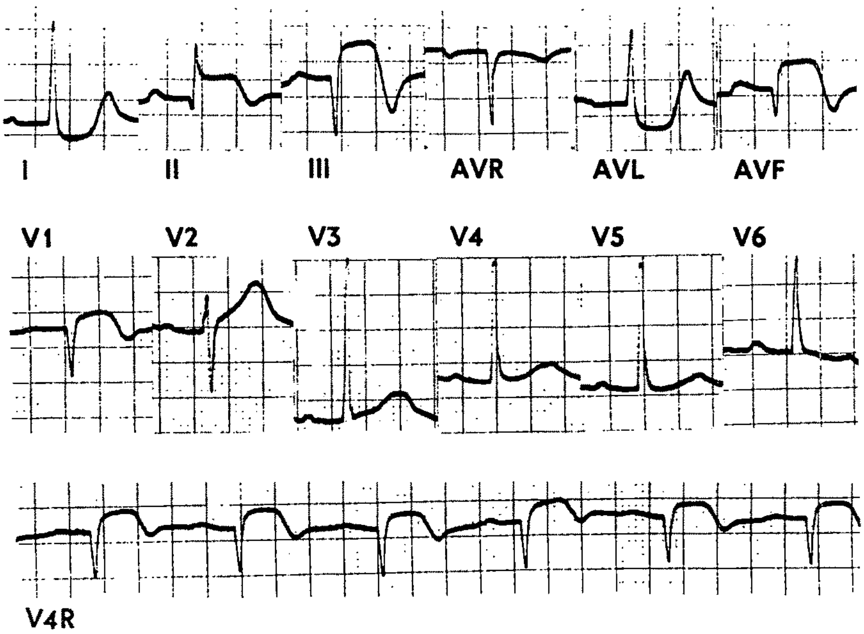


Figure 1. The electrocardiogram (EKG) of a 56-year-old man with an angiographically proven occlusion of the right coronary artery and subsequent acute myocardial infarction. This EKG shows infarction of the free wall of the right ventricle, as suggested by the curved and elevated ST segments in leads V and V_4R. (*From* Lynch C: Perioperative right ventricular ischemia. J Cardiothorac Anesth 1:126–131, 1987; with permission.)

end-diastolic volume and pressure measurements. A poor correlation exists between left ventricular end-diastolic volumes and left ventricular end-diastolic pressure relationships.[11,18] This may be analogous to studies reporting a poor correlation between left ventricular volume and pressure. This poor correlation between left ventricular end-diastolic volume and pulmonary artery wedge pressure has been demonstrated by Hansen et al.[25] They studied the relationship between left ventricular end-diastolic volume (gated blood pool scintigraphy) and stroke volume (determined by thermodilution) in cardiac surgical patients. In post-coronary artery bypass patients, there is a poor correlation between changes in pulmonary wedge pressure and left ventricular end-diastolic volumes. It is likely that an analogous relationship exists between RV pressure and RV volume.

Several of the same diagnostic and therapeutic modalities that have been developed for the evaluation of left ventricular volume have also been employed for the measurement of RV volume. However, because of the anatomic variability of the RV, development of a standardized technique that relies on development on a single geometric model is often difficult. Anatomically, the right ventricle is a crescent-shaped structure with a variable shape which is determined by loading conditions. Depending on the angle from which it is viewed (that is, superior, inferior, or apical), the RV has been described as a pyramid, an ellipse, or a tetrahedron. Present techniques available for evaluation of RV volume include angiography, echocardiography, radionuclear methods, thermodilution, and, recently, nuclear magnetic resonance imaging. However, because of logistical and technical constraints, the use of several of these techniques is often limited in the operating room and intensive care unit. Angiography can pose a significant risk due to the pharmacologic properties of currently available contrast media. Each study necessitates the injection of additional dye with a subsequent osmotic load which may be poorly tolerated by seriously ill patients.[2,40,45]

In an attempt to avoid some of the problems encountered with angiography, radionuclear techniques have been employed. Two commonly used radionuclear techniques are the first pass technique and the equilibrium gated pool scan. Both techniques allow for the determination of several parameters including ejection fraction, systolic ejection time, peak filling rates, peak ejection fraction, and rate of contractility.[3,17,42,43] The first pass technique facilitates the measurement of these parameters during a single cycle and is based on the principles of indicator dilution therapy. Homogeneous mixing of the radioactive trace is necessary for proper performance of this technique. Therefore, any artifact encountered, for example, arrhythmias, may invalidate the results obtained using this method. Also, a separate injection of radioactive agent is required for each first pass study and, as a result, patients may be subjected to a large amount of radiation if serial studies are needed. To avoid problems associated with repeated measurements, development of new half short live traces such as gold 195m may allow numerous sequential first pass studies to be performed without the accumulation of radiotracer.[55] The equilibrium gated pool uses labeled red cells for evaluation of RV function and allows for repeated measurements with only a single bolus injection of radioactive tracer.[17,39] By use of a computer, approximately 5 minutes of heart beats are collected and gated to the EKG, an averaged cycle constructed presents RVEF. The left anterior oblique (LAO) projection is most often used in order to clearly separate the counts obtained from the two ventricular chambers. However, even with this orientation there is a high degree of superimposition of the right atrial activity, as high as 20 per cent in some studies. Despite their limitations, these two radionuclear methods have been used very effectively for the evaluation of right ventricular function.

In addition to the previously mentioned radionuclear techniques, both M-mode and two-dimensional echocardiography have been employed to investigate right ventricular function.[9,12,35,47] Ultrasound provides useful information regarding (1) the thickness of the anterior-posterior free wall, (2) RV dimensions, and (3) the motion of the IVS, which may reflect the loading conditions.[9,47,58] M-mode echocardiography provides only an "ice pick" view of the RV. That is, by using a single beam of sound this technique generates a "one-dimensional recording" that lacks spatial orientation.

In contrast to M-mode, two-dimensional echocardiography using multiple beams of sound allows simultaneous visualization of larger areas of the right ventricular cavity.[9,22,58] This technique allows the construction of a more spatially correct image of the heart. Examinations are recorded from a standard apical four-chamber view, parasternal short-axis view at the tricuspid valve, and the subcostal long-axis view. The apical four-chamber view has been most extensively studied and appears to provide the most useful information.[35] Linear dimensions, such as right ventricular long and short axis, as well as anterior and posterior dimensions can be measured and systolic shortening calculated. Several mathematical models have been proposed for calculating end-diastolic volume, end-systolic volume and derived ejection fraction.[21,45] Owing to the inherent difficulty in developing a simple geometric model of the RV, regression equations may inaccurately predict ventricular volumes. Several methods, including Simpson's rule, have been proposed to determine RV volumes from echocardiographic data.[58] However, these methods may over-estimate right ventricular volume by as much as 20 to 40 per cent. Therefore, echocardiographic assessment of qualitative evaluation of RV ventricular function has several limitations. These are related to the shape of the RV cavity and its position directly below the sternum which acoustically "hides" the RV. In addition, none of these methods allows for the change in RV shape that occurs during volume loading.[22,57]

Recently, two-dimensional transesophageal echocardiography has been used to monitor intraoperative myocardial performance. Although initially developed to access LV dynamics, this technique may prove to be beneficial in assessing RV performance. The position of the two-dimensional transesophageal probes avoids the problem associated with sternal interference seen with the other echocardiographic techniques. Terai et al recently reported the effects of positive end-expiratory pressure (PEEP) on cardiac function using two-dimensional transesophageal echocardiography.[49] Measurement of RV function during PEEP demonstrated a decrease in right ventricular and preload (PEEP > 15 cm H_2O).

In an attempt to overcome the limitations of the previously described techniques, a new technique has been developed to determine RV volumes. Based on the indicator dilution theory and use of the rapid response thermistor pulmonary artery flow catheter, right ventricular ejection fraction (RVEF) can be calculated (Fig. 2).[4] The thermistor response, of the standard thermistor-tipped pulmonary artery catheter, is between 300 and 1000 ms. By reducing the response time to 50 ms (rapid response thermistor), beat-to-beat temperature variation may be seen on a thermodilution cardiac output curve. A typical thermal washout cardiac output curve generated by this method allows measurement of changes in temperature associated

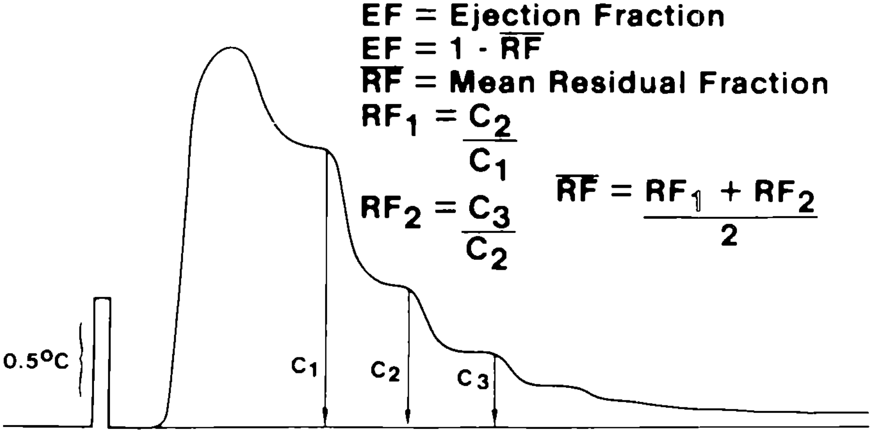


Figure 2. Thermal dilution cardiac output curve obtained with a rapid response pulmonary artery catheter. Following 0.5°C calibration spikes, a thermal bolus is injected. Plateaus represent diastolic C_1, C_2, and C_3 temperature differences between respective diastolic plateaus. (*From* Kay H, Afshan M, Barash PG, et al: Measurement of ejection fraction by thermal dilution techniques. J Surg Res 34:337–346, 1983; with permission.)

with successive diastolic plateaus (Fig. 2).[52] Computation of the right ventricular ejection fraction (RVEF) is then easily accomplished. (Normal thermodilution RVEF is approximately 40 per cent).

RV stroke volume = cardiac output/heart rate
RV end-diastolic volume = RV stroke volume/RV ejection fraction
RV end-systolic volume = RV/end-diastolic volume—RV stroke volume

In addition to RVEF, stroke volume, end-diastolic volume, and end-systolic volumes may also be easily calculated using this method. This catheter provides cardiac output, right ventricular ejection fraction, pulmonary artery and capillary wedge pressure, and right ventricular pressure as well as right atrial pressures.

Kay and colleagues have validated this technique using radionuclear studies in both an animal model and in patients following open heart surgery.[32] Subsequent validation of the thermodilution determination of RV volumes and ejection fraction measurements has been performed using biplane angiography by Urban et al.[51] There are, however, two specific limitations to the use of this technique. The first involves patients with cardiac dysrhythmias, such as atrial fibrillation. Variations in diastolic filling time may introduce the errors into the measurement of right ventricular ejection fraction. However, as the RVEF is computed within four to five beats, an average RVEF may be obtained. In addition, in patients with regurgitant valvular lesions, especially tricuspid insufficiency, an erroneous RVEF may be seen since this technique measures only forward flow. However, placement of a thermistor in the atrium will allow calculation of the regurgitant fraction.

Techniques of nuclear magnetic imaging have recently been employed as a new method for assessing myocardial performance. Evaluation of the right ventricle using magnetic resonance imaging was recently described by Machiewicz et al.[38] This technique was extremely effective in its ability to evaluate RV architecture and size. In addition, the tricuspid valves, as well as end-systolic and end-diastolic RV volumes were easily visualized. In addition, magnetic resonance imaging provided clear epicardial surfaces which will be useful for qualitative and quantitative assessment of the complex RV geometry.

The importance of monitoring RV function becomes apparent in several clinical situations. These include patients with adult respiratory distress syndrome, patients with chronic obstructive pulmonary disease, patients requiring mechanical ventilation, patients receiving an infusion of protamine, and patients with right coronary artery disease. Matthay and his colleagues have identified the presence of RV dysfunction in patients with chronic obstructive pulmonary disease using radionuclear stress testing.[41] Their report documents the importance of the evaluation of RV performance in this higher risk group of patients. In their series of 30 patients, only 8 had evidence of RV dysfunction at rest. However, in response to exercise, abnormal elevations of RV systolic and diastolic pressures were evident in 23 patients.

In the management of patients with adult respiratory distress syndrome (ARDS), knowledge of RV function is also clinically important. Regardless of the etiology of ARDS, RV dysfunction usually occurs as a result of increasing afterload, secondary to pulmonary artery hypertension. Sibbald et al examined biventricular function in patients with ARDS and found a negative correlation between right ventricular ejection fraction and the mean pulmonary artery pressure.[48] This increase in pulmonary artery pressure has also been associated with a depression of RV contractility. It has been proposed that with increasing RV end-diastolic volume an increase in RV wall stress may develop that may predispose the RV to subendocardial ischemia. The degree of pulmonary artery hypertension necessary for the development of ischemia and resultant RV failure has not been determined.

Much debate has centered on the practice of using volume expansion as the primary treatment modality in the setting of acute respiratory failure with associated pulmonary hypertension. Prewitt et al investigated the hemodynamic effects of fluid therapy in the setting of increased RV and ARDS.[43] Using equilibrium scintigraphic techniques, the end-diastolic and systolic areas of both the left and right ventricles were measured. When pulmonary vascular resistance (PVR) was normal, volume loading resulted in an increased cardiac output. However, when increased PVR (that is, PA pressure) was present, volume expansion resulted in RV failure, documented by decreasing cardiac output and an increase in right ventricular end-diastolic pressure. They postulated that the increases in PVR, in combination with increased RV volumes, resulted in increased RV wall stress and a subsequent decrease in RV contractility. Thus, volume expansion further increased myocardial oxygen requirements, leading to RV dysfunction secondary to ischemia. In summary, ARDS complicated by pulmonary artery hypertension (PAH) is associated with the reduction in RVEF and an increase in RV end-diastolic volumes and may be associated with RV contractile dysfunction.

Various modes of mechanical ventilation may also impair RV performance. Braunwald et al have demonstrated that a gradient is developed during mechanical ventilation between transthoracic and transpulmonary pressures.[10] This results in a translocation of the central venous blood volume to the periphery, leading to a decreased venous return. Increases in transpulmonary pressure during mechanical ventilation increase lung volume and may exponentially increase pulmonary vascular resistance.[24] By increasing RV afterload, changes in ventilatory mode may influence right heart hemodynamics. Jardin has shown that mechanical ventilation with PEEP (30 cm H_2O) results in a shift of the intraventricular septum with paradoxical motion resulting in right heart dilatation and decreased left ventricular chamber size.[31] New data also reveal that in postoperative ventilated patients, a decrease in RVEF is seen at PEEP levels greater than 15 cmH_2O.[6] Further changes in ventilatory modes (that is, IMV or assist control) may further alter right heart function. Studies demonstrate that RVEF is most impaired with assist controlled ventilation and is least affected by intermittent mandatory or spontaneous ventilation.[7] These differences observed in the various modes of mechanical ventilation are thought to occur as the result of the differences that are obtained in intrathoracic pressure gradients.[24]

Recently, high-frequency jet ventilation has been reported to cause less hemodynamic instability than traditional modes of mechanical ventilation. However, its effect on right ventricular performance had not been fully evaluated until a recent report by Biondi et al.[5] They demonstrated the effect of airway pressure on RVEF. A significant negative correlation was seen between RVEF (thermal) and increasing amounts of airway pressure delivered by the high-frequency jet ventilator.

The effect of RV ischemia and/or infarction on global cardiac performance is currently under investigation. A recent investigation evaluated right ventricular function in patients undergoing coronary artery bypass surgery.[27a] Based on angiographic data, patients were classified according to the degree of stenosis present in the right coronary artery (RCA). Subsets were defined as those having less than 90 per cent stenosis and those with greater than 90 per cent stenosis of the right coronary artery. In the group of patients with greater than 90 per cent stenosis of the RCA a statistically significant increase in RVEF was observed following coronary artery revascularization. In a subsequent report, a patient with total RCA occlusion was observed to develop RV ischemia while undergoing cardiac surgery. The earliest signs of this right ventricular dysfunction are manifest as an elevation in right ventricular end-diastolic pressure accompanied by a decrease in RVEF (in the face of a normal PCWP).[27b] This loss of RV compliance was not seen on electrocardiography using a cumulation of II and V_5. The administration of intravenous nitroglycerin resulted in the induction of this event (Fig. 3).

The importance of monitoring RV function intraoperatively has been illustrated by recent reports of RV failure following protamine infusion. Protamine administration has been associated with RV failure and subsequent cardiac decompensation.[36] Numerous studies imply a predominant vasodilating response as the principal event responsible for myocardial dysfunction following protamine administration.[15] However, a report by Lowenstein suggests that pul-

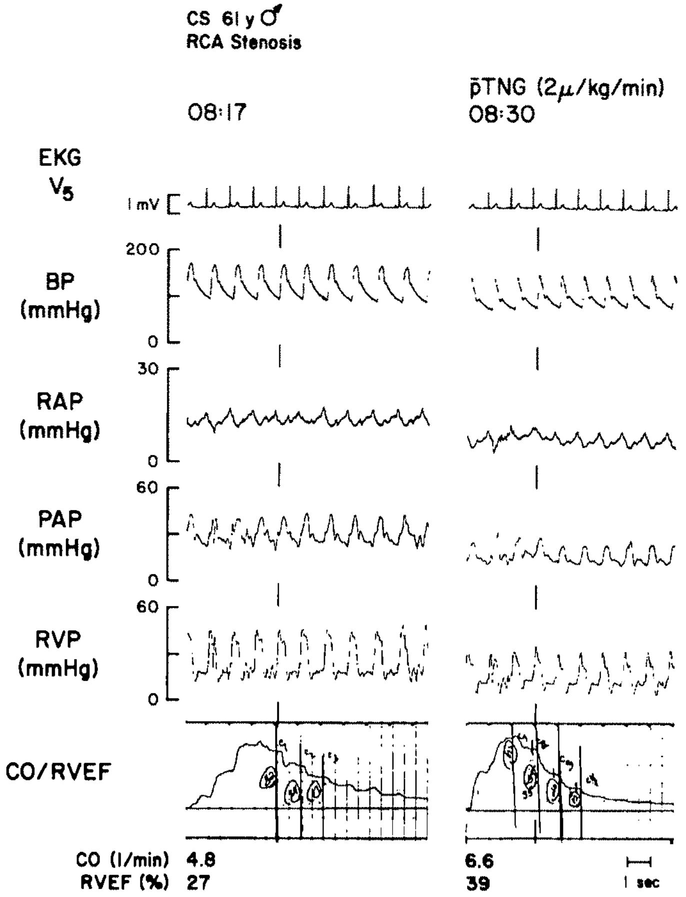


Figure 3. Loss of RV compliance in a patient with dominant right coronary artery disease is seen with increasing RV end-diastolic pressure and decreasing RVEF. Nitroglycerin resulted in resolution of these events. EKG leads II (not shown) and V_5 failed to show RV ischemia. EKG = electrocardiogram, BP = blood pressure, RAP = right atrial pressure, PAP = pulmonary artery pressure, RVP = right ventricular pressure, CO = cardiac ouptut, p̄NTG = post nitroglycerin therapy. (*From* Hines R, Barash PG: Intraoperative right ventricular dysfunction detection with a right ventricular ejection fraction catheter. J Clin Monitoring 2:206–208, 1986; with permission.)

monary vasoconstriction following protamine infusion is the primary event leading to RV failure.[36] Lowenstein described five patients who developed severe hemodynamic instability when intravenous protamine was infused following cardiopulmonary bypass. To ascertain if protamine infusion was associated with alterations in RV performance on an episodic or consistent basis, Hines and Barash evaluated both right and left ventricular function in patients undergoing open heart surgery.[28] No statistically significant changes in RVEF, RVEDP, systemic blood pressure, mean pulmonary artery pressure, or pulmonary vascular resistance were seen at any point during the study. In the patients undergoing coronary artery bypass surgery, right ventricular end-diastolic pressure did not significantly increase from the baseline. Similarly, in the patients with valvular heart disease, the preprotamine right ventricular end-diastolic pressure remained unchanged throughout the study. These values remained statistically unchanged following protamine infusion. In addition, no statistically significant alterations in left ventricular function could be detected in the cardiovascular response to protamine within either patient population. To ascertain whether pulmonary artery hypertension was an additional risk factor, they examined right and left ventricular function in a subset of patients with pulmonary artery hypertension (PAP greater than 25 mm Hg). Even in these high-risk patients, right ventricular performance as measured by RVEDP and RVEF failed to reveal any predictable deterioration in RV function during or following protamine infusion.

As new evidence demonstrating the importance of RV function becomes available, diagnostic and therapeutic strategies will continue to be developed to ensure detection and the rapid treatment of RV dysfunction. Employing this combination of early diagnosis and treatment, overall cardiac performance can be maximized in critically ill patients.

REFERENCES

1. Alpert JS, Braunwald E: Pathological and clinical manifestations of acute myocardial infarction. *In* Braunwald E (ed): Heart Disease: A Textbook of Cardiovascular Medicine. Philadelphia, W.B. Saunders, 1984, pp 1268–1274
2. Arcilla RA, Tsai P, Thilenius O, et al: Angiographic method for volume estimation of right and left ventricles. Chest 446–454, 1971
3. Bailey IK, Griffith LSC, Rouleau J, et al: Thallium-201 myocardial perfusion imaging at rest and during exercise: Comparative sensitivity to electrocardiography in coronary artery disease. Circulation 55:79–87, 1977
4. Bing R, Heimbecker R, Falholt W: An estimation of the residual volume of blood in the right ventricle of normal and diseased human hearts in vivo. Am Heart J 42:483–502, 1951
5. Biondi J, Hines R, Rafferty T, et al: The effect of high frequency positive pressure ventilation on right and left ventricular function. Anesth Analg 65:679–682, 1986
6. Biondi JW, Hines RL, Barash PG, et al: The effect of PEEP on right ventricular function. Ann Rev Resp Dis 133:303–307, 1986

7. Biondi JW, Hines RL, Matthay RA, et al: Comparative right ventricular function during assist control, intermittent mandatory and spontaneous ventilation. Anesth Analg 65:518, 1986
8. Blackburn H: The exercise electrocardiogram: Technological, procedural and conceptual development. *In* Measurements in Exercise Electrocardiography. Springfield, IL, Charles C Thomas, 1964
9. Bommer W, Weinert L, Neuman A, et al: Determination of right atrial and ventricular size by two-dimensional echocardiography. Circulation 60:91, 1979
10. Braunwald E, Binan JT, Morgan WL, et al: Alterations in central blood volume and cardiac output induced in PEEP and characterized by metaramine (aramine). Circ Res 5:675, 1957
11. Calvin JE, Driedger AA, Sibbald WJ: Does the pulmonary capillary wedge pressure predict left ventricular preload in critically ill patients? Crit Care Med 9:437–443, 1981
12. Chaudry KR, Ogawa S, Pauletto FT, et al: Biplane measurement of left and right ventricular volumes using wide-angle cross sectional echocardiography. Am J Cardiol 41:391–404, 1978
13. Chou T, Van Der Bel-Kahn J, Allen J, et al: Electrocardiographic diagnosis of right ventricular infarction. Am J Med 70:1175–1180, 1981
14. Cohn JN, Guiha NH, Broder MI: Right ventricular infarction. Am J Cardiol 33:209–214, 1974
15. Corchran TJ III, Andrews RW, MacVaughn III: Cardiovascular effects of protamine sulfate in man. Anesth Analg 60:33–36, 1981
16. Croft CH, Nicod P, Corbett JR, et al: Detection of acute right ventricular infarction by right precordial electrocardiography. Am J Cardiol 50:421–427, 1983
17. Dehmer GJ, Firth BG, Hills LO, et al: Nongeometric determination of RV volume from equilibrium blood pool scans. Am J Cardiol 49:78–84, 1982
18. Ellis RJ, Mangano DT, Van Dyke DC: Relationship of wedge pressure to end-diastolic volume in patients undergoing myocardial revascularization. J Thorac Cardiovasc Surg 78:605–613, 1979
19. Erhardt LF, Sjogren A, Wahlberg I: Single right-sided precordial lead in the diagnosis of right ventricular involvement in inferior myocardial infarction. Am Heart J 91:571–576, 1976
20. Ferlinz J, Delvicario M, Gorlin R: Incidence of right ventricular asynergy in patients with coronary artery disease. Am J Cardiol 38:557–560, 1976
21. Ferlinz J: Measurement of right ventricular volumes in man from single plane cineangiograms. Am Heart J 94:87–91, 1977
22. Fischer EQ, Du Brow IW, Hastreiter AR: Right ventricular volume in congenital heart disease. Am J Cardiol 36:67–71, 1975
23. Geft IL, Shah PK, Rodriquez L: ST elevations in leads V_1 to V_5 may be caused by right coronary artery occlusion and acute right ventricular infarction. Am J Cardiol 53:991–996, 1984
24. Hagnes JB, Carlson SD, Weuling WP, et al: Positive end-expiratory pressure shifts in left ventricular diastolic pressure area curves. J Appl Physiol 48:670–676, 1979
25. Hansen MD, Viquerat CE, Matthay M, et al: Poor correlation between pulmonary arterial wedge pressure and left ventricular end diastolic volume after coronary artery bypass graft surgery. Anesthesiology 64:764–770, 1986
26. Haupt MM, Hutchins GM, Moore GW: Right ventricular infarction: Role of the moderator band artery in determining infarct size. Circulation 67:1268–1272, 1983

27a. Hines R, Barash PG: Right ventricle: Master or servant? Anesthesiology 61:A8, 1984

27b. Hines R, Barash PG: Intraoperative right ventricular dysfunction detection with a right ventricular ejection fraction catheter. J Clin Monitoring 2:206–208, 1986

28. Hines R, Barash PG: Protamine: Does it alter right ventricular performance? Anesth Analg 65:1271–1274, 1986
29. Hines R: Monitoring for right ventricular ischemia: Is it necessary? J Cardiothorac Anesth 95:97, 1987

30. Isner JM, Roberts WC: Right ventricular infarction complicating left ventricular infarction secondary to coronary heart disease. Am J Cardiol 42:885–894, 1978
31. Jardin F, Farcot JC, Boisanti C, et al: Influence of positive end expiratory pressure on left ventricular performance. N Engl J Med 304:387–392, 1981
32. Kay H, Afshan M, Barash PG, et al: Measurement of ejection fraction by thermal dilution techniques. J Surg Res 34:337–346, 1983
33. Klein HO, Tordjma T, Ninio R, et al: The early recognition of right ventricular infarction: Diagnostic accuracy of the electrocardiographic V_4R lead. Circulation 67:558–565, 1983
34. Lisa JR, Ring A: Myocardial infarction of gross fibrosis: Analysis of 100 necropsies. Arch Intern Med 50:131–141, 1932
35. Lopez Sendon J, Coma Canella I, Lombera F, et al: Diagnosis of ischemic right ventricular dysfunction by M-mode echocardiography. Eur Heart J 3:230–237, 1982
36. Lowenstein E, Johnson W, Lappas D, et al: Catastrophic pulmonary vasoconstriction associated with reversal of heparin. Anesthesia 59:470–473, 1983
37. Lynch C: Perioperative right ventricular ischemia. J Cardiothorac Anesth 1:126–131, 1987
38. Machiewicz W, Sechtem V, Higgins C: Evaluation of the right ventricle by magnetic resonance imaging. Am Heart J 113:8–15, 1987
39. Maddahi J, Berman DS, Matsuoka DT, et al: Technique for assessing right ventricular ejection fraction using rapid multiple-gated equilibrium cardiac blood pool scintigraphy: Description, validation and finding in coronary artery disease. Circulation 60:581–589, 1979
40. Marshall RC, Berger HJ, Costlin JC, et al: Assessment of cardiac performance with qualitative radionuclide angiocardiography: Sequential left ventricular ejection fraction, normalized left ventricular ejection rate and regional wall motion. Circulation 56:820–829, 1977
41. Matthay RA, Berger HJ: Cardiovascular performance in chronic obstructive pulmonary disease. Med Clin North Am 65:489–524, 1981
42. Meller J, Goldsmith S, Rudin A, et al: Spectrum of exercise thallium-201 myocardial perfusion imaging in patients with chest pain and normal coronary arteries. Am J Cardiol 43:717–723, 1979
43. Prewitt R, Ghignone M: Treatment of right ventricular dysfunction in acute respiratory failure. Crit Care Med 5:346–352, 1983
44. Reddy GV, Schamroty L: The electrocardiology of right ventricular myocardial infarction. Chest 90:756–760, 1987
45. Reedy T, Chapman CB: Measurement of right ventricular volumes by cineangiography. Am Heart J 66:221–225, 1963
46. Ritchie J, Zaret B, Strauss H, et al: Myocardial imaging with thallium 201: A multicenter study in patients with angina pectoris or acute myocardial infarction. Am J Cardiol 42:345–350, 1978
47. Sharpe DW, Botvinick EH, Shames DM, et al: The non-invasive diagnosis of right ventricular infarction. Circulation 57:483, 1978
48. Sibbald WJ, Paterson NA, Holliday NL, et al: Pulmonary hypertension in sepsis. Measurement of the pulmonary artery diastolic-pulmonary wedge pressure gradient and the influence of passive and active factors. Chest 73:583–591, 1978
49. Terai C, Venigh M, Sugimato H, et al: Transesophageal echocardiographic dimensional analysis of four cardiac chambers during positive end expiratory pressure. Anesthesiology 63:640–646, 1985
50. Trager M, Feinberg B, Kaplan J: Right ventricular ischemia diagnosed by an esophageal echocardiogram and right atrial pressure tracing. J Cardiothorac Anesth 1:123–126, 1987
51. Urban P, Scheldegger D, Gabathuler J, et al: Thermodilution determination of right ventricular volume and ejection fraction: A comparison with byplane angiography. Crit Care Med 15:652–655, 1987
52. Vincent JL, Thirion M, Brimioulles P, et al: Thermodilution measurement of right ventricular ejection fraction with a modified pulmonary artery catheter. Intensive Care Med 12:33–36, 1986

53. Virmani R, Foiman MB, Gooddin J, et al: Electrocardiographic changes associated with isolated right ventricular function. J Am Coll Cardiol 4:640–643, 1984
54. Virmani R: Right ventricular myocardial infarction in patients with chronic lung disease: Possible role of right ventricular hypertrophy. J Am Coll Cardiol 5:1302–1307, 1985
55. Wackers FJ, Giles RW, Hoffer PB, et al: Gold 195m, a new generator produced short lived radionuclear tracer for sequential assessment of ventricular performance by first pass radionuclide angiocardiography. Am J Cardiol 50:89–94, 1987
56. Wellens HJJ: Value of lead V_4R in exercise testing to predict proximal stenosis of the right coronary artery. J Am Coll Cardiol 5:1308–1311, 1985
57. Weyman AC, Wann LS, Frigenbaum H, et al: Mechanism of abnormal septal motion in patients with right ventricular volume overload. Circulation 54:179–183, 1976
58. Weyman AE: Right ventricle. *In* Weyman AE (ed): Cross Sectional Echocardiography. Philadelphia, Lea & Febiger, 1982, pp 382–395

Department of Anesthesiology
Yale University School of Medicine
333 Cedar Street
New Haven, CT 06510

0889-8537/88 $0.00 + .20

Monitoring Intravenous Infusion and the Venous Circulation

*James H. Philip, MD**

Recent laboratory tests and limited patient studies have given us new insights into intravenous (IV) fluid administration and the venous circulation.[18] These insights show that the laws of physics that are familiar in other situations[1,6,12] also apply when fluid is infused through IV systems into patients. Our new insights provide a physical and mathematical model that describes how pressure, resistance, and flow are related in IV fluid administration.

The technology of IV fluid administration has progressed rapidly and persistently during the past 30 years. Although conventional roller-clamp control is still used in most operating rooms, intensive care units (ICUs) and other patient care areas rely heavily on IV controllers and pumps in an attempt to enhance patient care. Unfortunately, the advantages and disadvantages of different techniques and devices have been obscure. This is largely because we failed to understand the physics and physiology involved.

Commercial infusion systems have evolved in a seemingly logical manner: Initially, IV fluid administration systems were composed of an elevated bag or bottle of fluid, a length of plastic tubing compressed at one site by a roller clamp, a catheter, and the patient's vein.[21] Clinical observations showed that flow rate was inaccurate[3,11] and varied spontaneously[4]; this was attributed to changes in the shape of the plastic tubing within the clamp ("cold flow") or movement of the roller ("clamp creep"). In an attempt to solve the problem of flow variation, "creepless" clamps were manufactured using improved design and materials, but flow still varied.[26] It was then reasoned that changes in flow rate, under otherwise constant conditions, must be due to "patient factors." Clinicians had already learned to compensate for flow variation by frequently checking and readjusting flow rate. To maintain constant flow manually, either clamp resistance or bag height were adjusted. In the early 1970s, electronic IV rate controllers were first introduced.[8] Most of these devices automatically varied clamp resistance by compressing the tubing. One instrument varied effective bag height by intermittently occluding the tubing (IVAC Model 260, IVAC Corporation, San Diego, CA). These IV flow controllers were able to achieve accurate consistent flow,[8,22] and some even provided the clinician with information to help manage the IV site. Other nonindicating devices simply regulated flow while they actually obscured patient changes.

---

*Anesthesiologist and Director of Bioengineering, Department of Anesthesia, Brigham and Women's Hospital; Assistant Professor of Anaesthesiology, Harvard Medical School and Harvard-MIT Division of Health Sciences and Technology, Boston, Massachusetts

Occasionally, IV controllers were unable to deliver the set flow rate using only the pressure available from the height of the fluid container and sounded an alarm instead. The advent of the IV infusion pump answered the need for a more robust fluid administration system, capable of delivering the desired volume and flow regardless of pressure required.[8] However, the use of IV pumps sometimes led to severe tissue damage when necrotizing agents as diverse as KCl, dopamine, calcium salts, and Adriamycin (doxorubicin)[13,24,25] were infiltrated into extravascular compartments.

Incorporation of a medical-grade pressure transducer and microprocessor into one manufacturer's product (Variable-Pressure Volumetric Infusion Pump Model 560, IVAC Corporation, San Diego, CA)[7,20] affords some protection. With the pressure-monitoring pump, when infusion pressure exceeds the preset level, an alarm sounds and flow is interrupted. Nonetheless, even with such a sophisticated pressure-monitoring instrument, infiltration still cannot be reliably detected or prevented.

In our laboratories at Brigham and Women's Hospital, we have created a physical model to explain the behavior of IV infusion systems. The model and its mathematics are described simply in the following pages.

In our experiments and in the following discussion, a commercially available infusion pump, capable of monitoring pressure while providing controlled flow, is used to make measurements that illustrate the model and give tremendous insight into understanding IV fluid administration. Using the model, its mathematics, and measurements made with the pressure-monitoring infusion pump, we believe we can detect infiltrations and distinguish them from artifacts and more minor IV site problems that cause partial obstruction.

THE RELATIONSHIP BETWEEN PRESSURE, RESISTANCE, AND FLOW

Figure 1 shows a gravity flow IV system with rate controlled manually by a roller clamp, which works by creating a large resistance to flow by constricting the tubing. The system is composed of an elevated fluid-filled bag, flow (F) down and through the tubing, the roller clamp, an IV catheter, the patient's vein (where resistance and collapse, that is, obstruction, affect), and the heart.

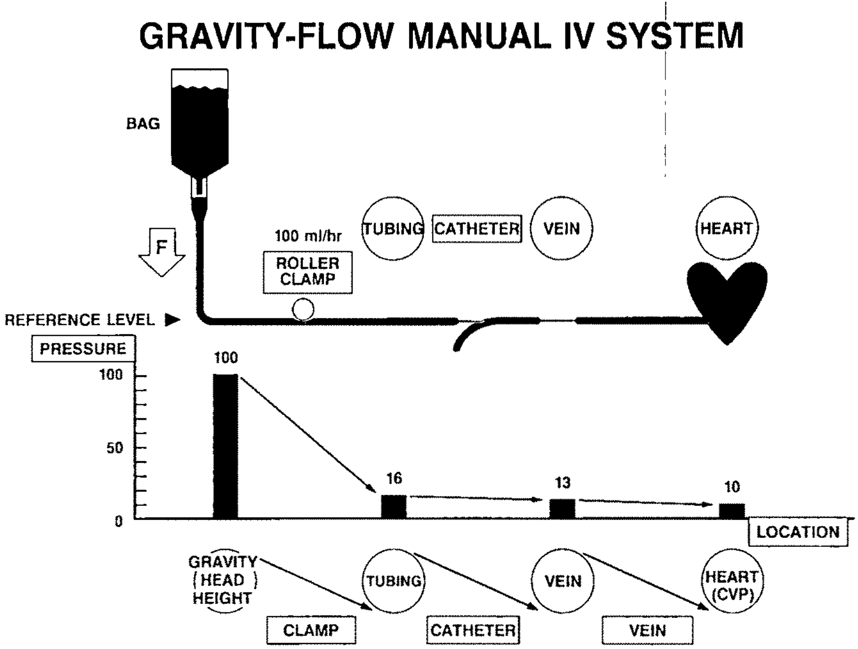


Figure 1. Gravity-flow manual IV system controlled by a roller clamp. *A)* Schematic diagram and *B)* typical pressures observed during 200 ml per hour flow into a patient through a 20-gauge catheter.

In Figure 1B we have constructed a scale that shows values obtained if we measure pressures within the combined tubing/patient system at several locations. A pressure scale on the left quantifies bar heights that depict pressures in the tubing, vein, and heart.

The pressure at the fluid level at the top of the bag is zero, or atmospheric pressure. However, the *height* of this fluid level is important because it represents the top of a column of fluid, which provides the motive force to cause flow. Gravity pulls down on the column causing it to flow through any outlet, "downhill," toward an area of lesser pressure. The bottom of this column is labeled the "reference level." The weight of the fluid column provides pressure at the reference level, which is proportional to the height of the column and the density (weight per unit volume) of the fluid. If the pressure is measured in cm H_2O, its value is equal to the height of the water level in the bag, measured in centimeters. Hydrostatic pressure is analogous to several circus gymnasts, each standing on the shoulders of the one below. The fellow on the top feels no pressure on his shoulders, but the one on the bottom feels the combined pressure of all the others above him. Therefore, with the fluid level 136 cm above, the pressure measured at the reference level would register 136 cm H_2O or 100 mm Hg.

The roller clamp in Figure 1 has been adjusted to 100 ml per hour by observing the rate of drop formation in the drip chamber and adjusting the roller clamp until the appropriate drop rate is attained. If a pressure measurement were taken between the roller clamp and catheter, the pressure might read 16 mm Hg. This would tell us that the resistance imposed by the roller clamp caused a large drop in pressure (from 100 to 16 mm Hg).

A measurement taken in the diagramed vein might read 13 mm Hg, indicating that a further pressure drop of 3 mm Hg occurred across the catheter.

Lastly, if we could measure pressure in the right atrium of the heart, "central venous pressure" (CVP) would read 10 mm Hg. This indicates a pressure drop of another 3 mm Hg within the veins.

Reviewing the whole model, we can see that the flowing infusion encountered a series of resistances that accounted for the entire pressure drop from 100 mm Hg (generated by the column head height) to 10 mm Hg at the heart. The pressures in this example are realistic. We especially note that the pressure of the fluid within the tubing, flowing at 100 ml per hour, is only 16 mm Hg.

In Figure 2, the roller clamp has been readjusted to a rate of 200 ml per hour. To permit the faster rate, the readjusted clamp offers less resistance, and the pressure measured in the tubing between the catheter and roller clamp is a bit higher, 22 mm Hg. The pressure in the vein is slightly higher than before, 16 mm Hg, and the pressure in the right atrium is unchanged at 10 mm Hg. Our 200 ml per hour flow

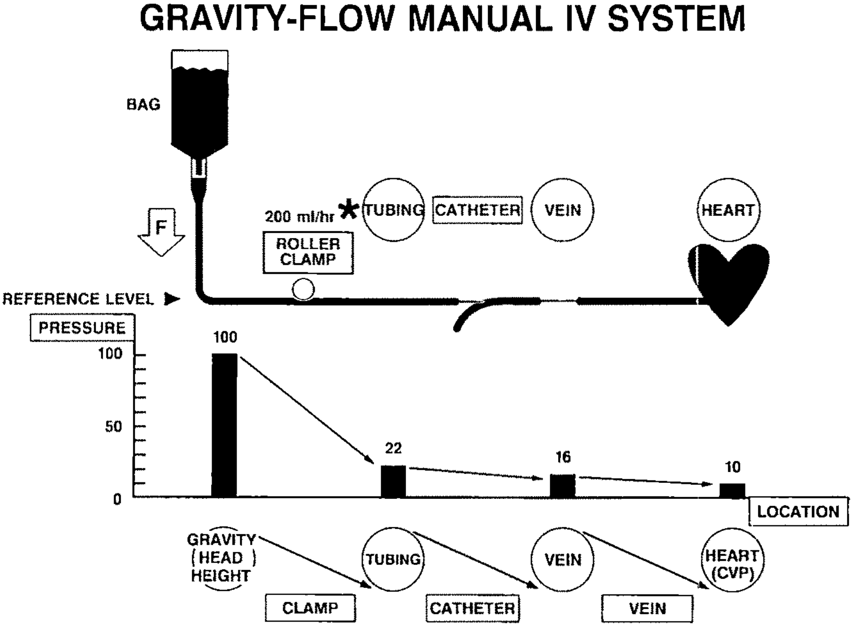


Figure 2. Model and pressures observed in a gravity-flow manual IV system with roller clamp adjusted to 200 ml per hour.

does not change the pressure in the patient's heart; however, we have changed the pressures observed at each point along the way. The *change in roller clamp resistance* altered pressures in the tubing on either side of the clamp and affected flow rate.

In Figure 3, we have further reduced the roller clamp resistance to allow flow to achieve 500 ml per hour. We notice that the pressure in the tubing has risen to 40 mm Hg, the venous pressure to 25 mm Hg, and the heart remains at 10 mm Hg.

During all the rate manipulations described, pressure provided by the 100 mm Hg gravity head height has remained constant, and we have observed that as resistance from the roller clamp was reduced, flow increased.

In Figure 4, the roller clamp is adjusted to stop flow completely. This action separates the patient/tubing system into two segments so that there is no longer a relationship between the pressures in the IV tubing above the clamp and downstream from it.

If we check the pressures at various sites in the system, we note that when there is no flow through a resistive component, there is no pressure drop across it. Therefore, we have learned that a resistor in a fluid path affects pressure only when there is flow present.

Further, since the clamp separates the downstream system from the bag as a pressure source, the pressure in the tubing segment beyond the clamp appears to originate from the patient's heart.

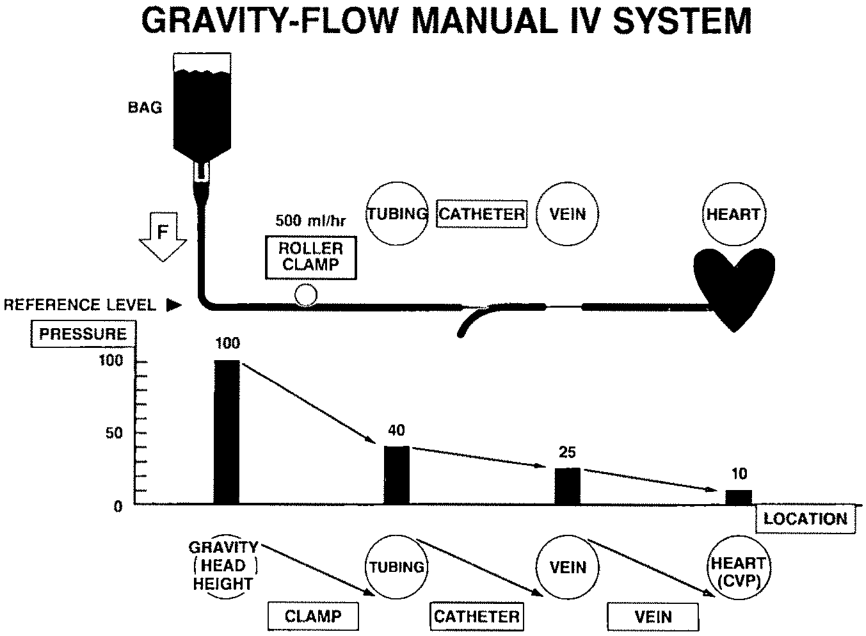


Figure 3. Model and pressures observed in a gravity-flow manual IV system with roller clamp adjusted to 500 ml per hour.

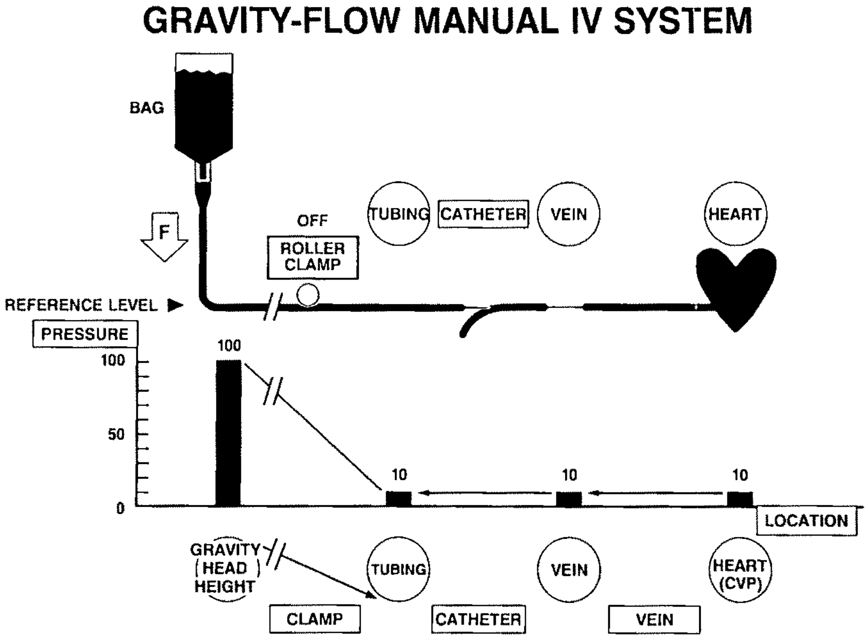


Figure 4. Model and pressures observed in a gravity-flow manual IV system with roller clamp turned completely off. Pressure measured arises from the patient's heart and is independent of bag height (see text for details and limitations).

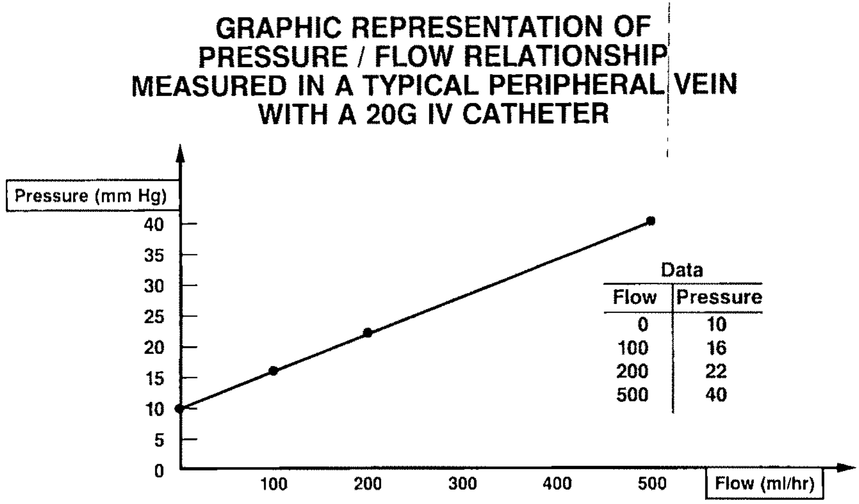
THE PRESSURE-FLOW RELATIONSHIP

Figure 5 depicts the pressure-flow relationship (PFR) for the system we have been discussing. The data table reminds us of the pressure measured in the tubing (between roller clamp and catheter) at each of the four flow rates, including zero.

When each pressure is marked on the graph directly above the corresponding flow rate, we observe that the points can be connected by a straight line. If we had measured the pressure at additional flow rates, they would have also fallen on this line that relates pressure to flow.

The PFR is a *property* or *characteristic* of the system we measured. In this case, the system comprised the fluid path from below the roller clamp to the patient's heart. As we will see, the slope of the PFR represents the total resistance (R) of this tubing-catheter-patient system. Resistance is one of the two crucial parameters in understanding IV fluid infusion.

By looking at the graph in Figure 5, we are reminded that the measured pressure at zero flow (P_0) was determined by the patient's CVP (heart), and that additional *resistive pressure* (P_{res}) resulted within the system only when there was flow through the resistors. Also, it is clear that P_{res}, the pressure resulting from resistance to flow, is proportional to flow.



Flow	Pressure
0	10
100	16
200	22
500	40

Figure 5. Graphic representation of the PFR measured in a typical peripheral vein with a 20-gauge IV catheter.

The PFR may be depicted in graphic form for any fluid path, component, or system. This is done by plotting pressures measured at two or more flow rates. Further, the PFR for a single tubing-catheter-patient system would be the same regardless of what provided the force to move the fluid (for example, gravity or pump) or what regulated the flow rate (clamp, controller, or pump). The pressure measured at any flow rate (P_F) is sometimes called "back pressure." If pressures and flows are measured with great accuracy over a wide range of flows, distinct nonlinearity is observed.[16,17] At the flow rates encountered here, nonlinearity is not significant.

Figure 6 demonstrates that the pressure (P_F) at any given flow rate (F), with the example system, is the sum of the stopped pressure (P_0), plus the resistive pressure (P_{res}) arising from flow through the system.

$$P_F = P_0 + P_{res} \tag{1}$$

Resistive pressure (P_{res}) arises from flow (F) and resistance (R):

$$P_{res} = R\,F \tag{2}$$

The PFR is described by the simple equation

$$P_F = P_0 + R\,F \tag{3}$$

The resistance for our example system is equal to the *slope* of the PFR (Fig. 7). Resistance is calculated by dividing the difference in pressures at any two flow rates by the difference in the flow rates:

$$R = \Delta P/\Delta F \tag{4}$$

$$R = P_{res}/F \tag{5}$$

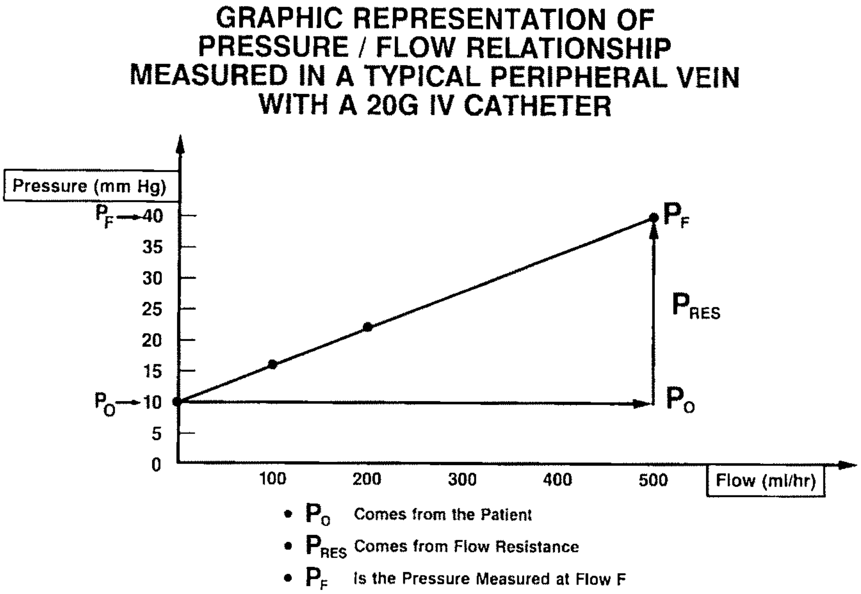


Figure 6. PFR demonstrating the origins of P_0, P_{res}, and P_F.

$$R = (P_F - P_0/F \tag{6}$$

We can calculate the resistance in our example system by looking at the resistive pressure caused by a flow rate of 500 ml per hour. To simplify the units for resistance, flow is expressed in liters per hour.

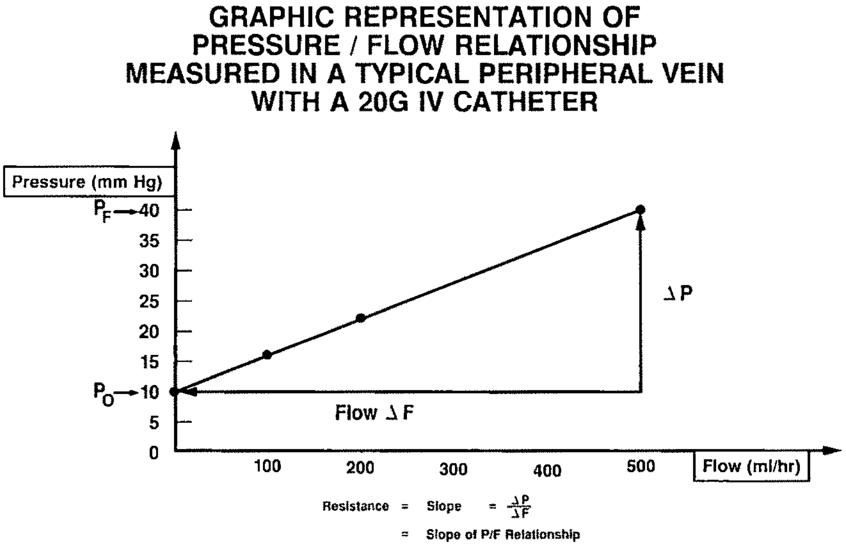


Figure 7. PFR demonstrating resistance is the slope of the PFR.

In Figure 8, the resistance of the system is R = $\Delta P/\Delta F = (P_F - P_0)/F$ = (40 mm Hg − 10 mm Hg)/(0.500 L per hour) = 30 mm Hg/(0.5 L per hour) = 60 mm Hg per L per hour = 60 resistive units. Resistive units (RU) are mm Hg per L per hour (Fig. 8). The units arise from dividing pressure (mm Hg) by flow (L per hour). These units refer to the slope of a line because the units describe the pressure rise expected for each 1 L per hour increase in flow rate.

In Figure 9, a volumetric pump replaces the roller clamp for rate regulation. Because the pump is a source of flow, the gravity head height is unimportant in this system; the pump draws fluid from the bag as needed to fulfill its volumetric pump cycle requirements. Therefore, the fluid column height is broken, showing it to be unrelated to the pressures in the system downstream.

As the pump drives the required flow through the system, *pressure results* because of resistance to flow from the downstream components. With the pump running at a flow rate of 200 ml per hour (Fig. 9), the pressure (P_F) that results in the tubing beyond the pump is 22 mm Hg. This pressure is equal to the pressure required to produce the same flow rate in our gravity flow example. This reinforces our earlier statement that the PFR for a single tubing-catheter-patient system will be the same regardless of the source of energy to move the fluid or of the type of device used to regulate flow. The term "back pressure" for P_F reminds us that P_F is the pressure that is produced when fluid is forced into the catheter and patient. In this forced-flow situation P_F appears to come *back* from the patient.

There is one commercial device that allows its pressure to be

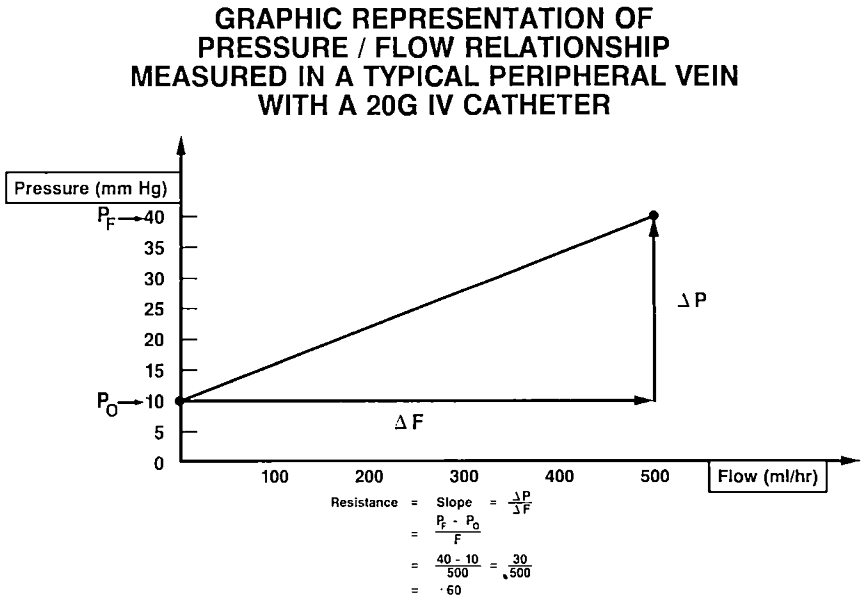


Figure 8. The PFR allows direct calculation of resistance.

VOLUMETRIC PUMP WITH PRESSURE MONITORING CAPABILITY (IVAC MODEL 560)

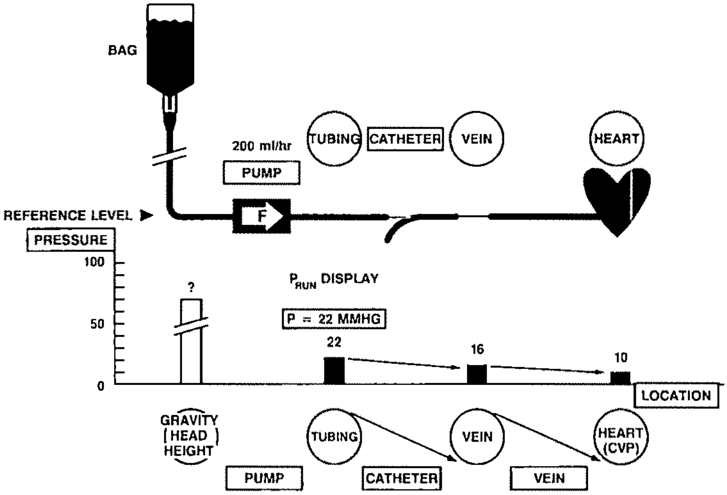


Figure 9. Model and pressures observed for a volumetric pump with pressure monitoring capability (IVAC Model 560). P_{run} is displayed on the instrument's front panel. Bag height plays no role in pressure considerations with IV pumps.

observed (Variable Pressure Volumetric Infusion Pump Model 560, IVAC Corporation, San Diego, CA). On the front panel of this instrument, the pressure used by the pump to achieve the set flow is displayed continuously as P_{run}. This value is a direct measurement of P_F.

In Figure 10, we observe in-line pressure when the pump is stopped and call this pressure P_{stop}. This value is a measurement of the parameter representing the intercept of the PFR with the pressure axis, namely P_0. When flow stops, if there is no obstruction in the vein or tubing, pressure equalizes between the pump and the patient's heart, as we observed when we closed the roller clamp in the gravity system. Therefore, the pressure measured in the tubing or the vein would equal pressure in the heart, the central venous pressure (CVP). Using the measured P_{run} and P_{stop} we can construct the same pressure-flow line that we had before, using only two points (Fig. 11).

$$P_{run} = P_{stop} + R\,F \tag{7}$$

We can then compute R and P_0:

$$R = \frac{P_{run} - P_{stop}}{F} \tag{8}$$

$$P_0 = P_{stop} \tag{9}$$

At F = 200 ml per hour, P_{run} was 22 mm Hg; and at zero flow, P_{stop}

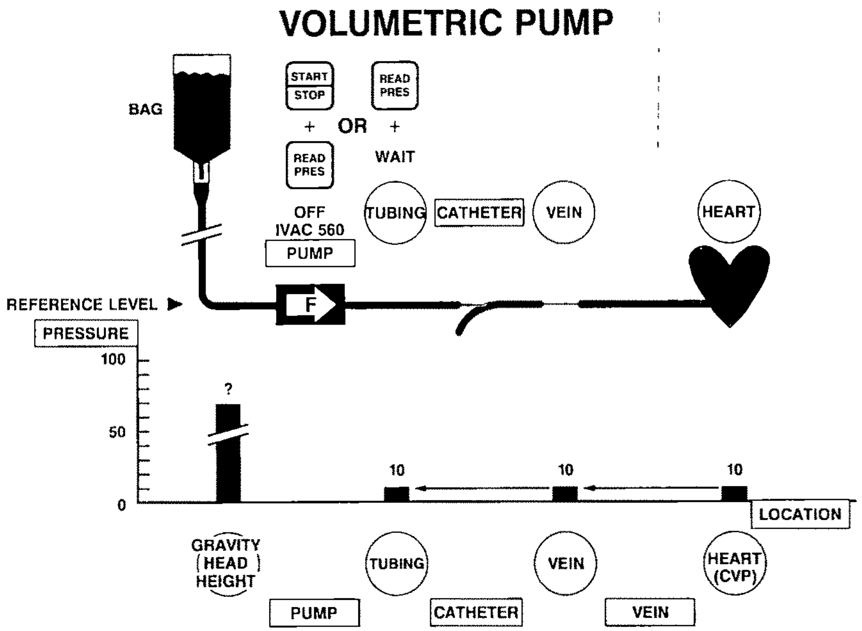


Figure 10. P_{stop} can be measured with the IVAC 560 by stopping flow and then pressing "READ PRESSURE" or by simply pressing "READ PRESSURE." For an unobstructed vein, P_{stop} = CVP.

was 10 mm Hg. Resistance may be calculated as $R = \Delta P/\Delta F = (P_{run} - P_{stop})/F = (22 - 10)/.200 = 12/.200 = 60$ mm Hg per L per hour.

In Figure 12, an automatic rate controller replaces the pump in the IV system. This controller regulates flow by mechanically varying

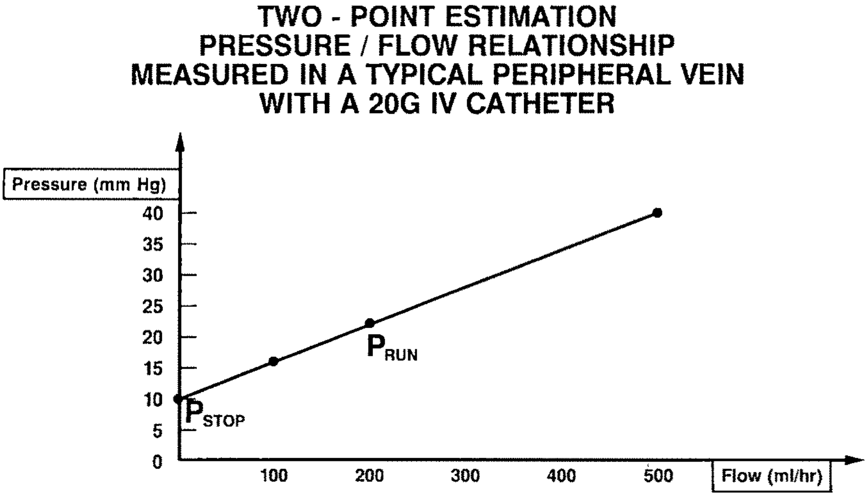


Figure 11. Two-point estimation of the PFR.

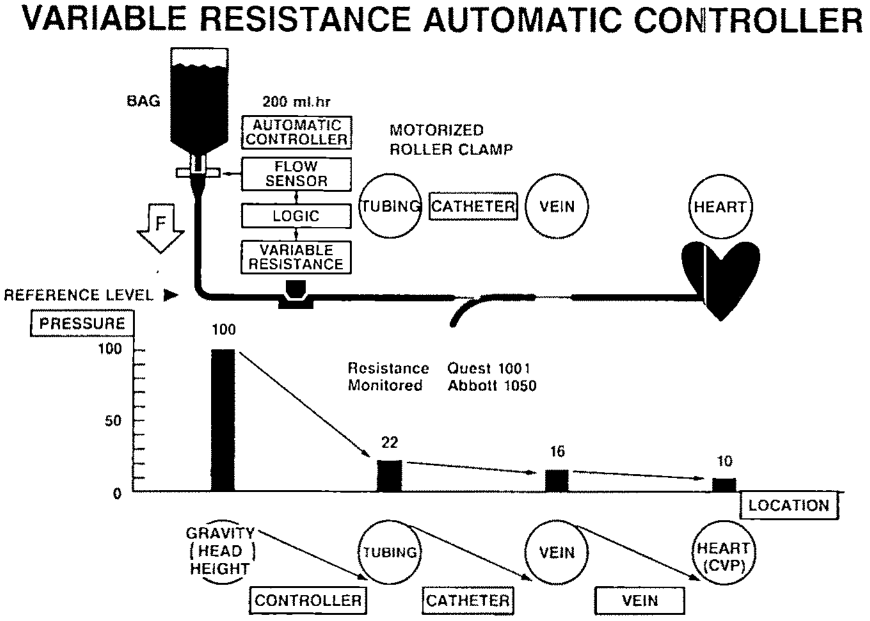


Figure 12. Model for and pressures observed with a variable *resistance* automatic controller.

the resistance imposed on the tubing. Resistance is varied until drop rate is measured to be equal to that desired, and set on the instrument. This variable resistance controller can be thought of as the automated version of a clinician continuously adjusting the roller clamp trying to keep drop rate constant. At 200 ml per hour, the pressure drop across each resistor and at each location in the system is the same as it was in the gravity-powered infusion earlier.

In this system, running pressure (P_{run}) cannot be measured or estimated by the instrument. Most resistance controllers do not attempt to display controller resistance, although two do have qualitative displays (Quest 1001, Abbott 1050).

The automatic rate controller depicted in Figure 13 (IVAC Model 230) regulates flow using a different principle; it modifies effective bag height (that is, effective pressure). With reference to the gravity head pressure, the pulsating pincer-anvil mechanism interrupts the pressure for a fraction of the total time, termed its "duty cycle." This "duty-cycle modulation" produces an effective pressure that is equal to the gravity head height times the fraction of the time the tubing is open. The fraction in turn is regulated by software plus flow data fed back from the flow sensor. During each moment when the pincer mechanism is open, flow occurs impeded only by tubing, catheter, and patient effects. Flow ceases when the pincer closes, only to reopen and allow flow just before the next drop is due. As patient resistance changes, the controller adjusts the fraction of time open versus closed. Adjustment of the effective pressure is reflected in the

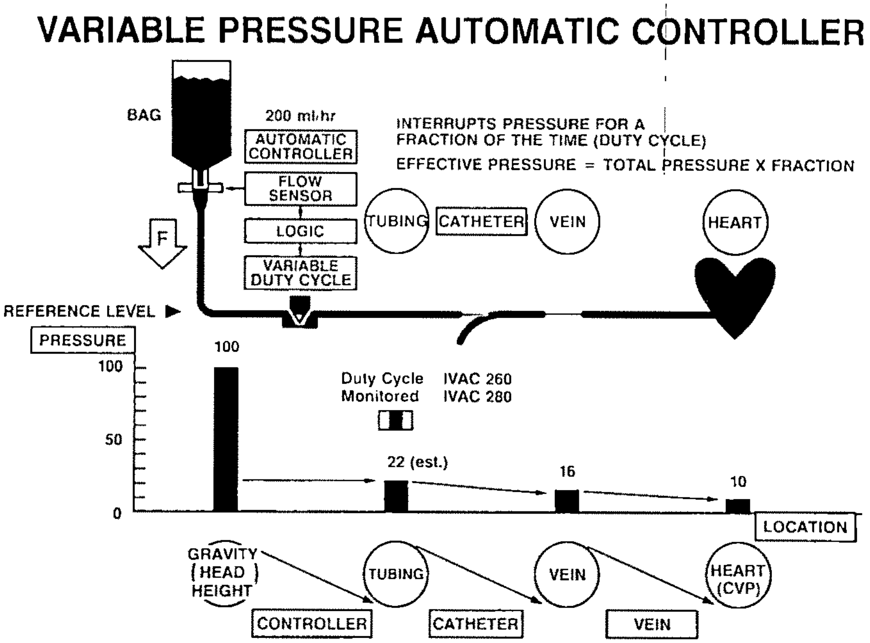


Figure 13. Model for and average pressures observed with a variable *pressure* automatic controller.

flow status light indicator panel, affording a means to monitor P_F qualitatively.

The aspect of reducing effective head height to some fraction of what might be expected from measuring the bottle height has advantages and disadvantages. Advantages include sensitivity to changes in patient resistance and less pressure available to force fluid into infiltrated tissues. A disadvantage is excess sensitivity to pressure artifacts. Of course, the bag height may be raised to decrease sensitivity or lowered to customize the head height for optimal flow status monitoring.

EXTRAVASATION (INFILTRATION) AND THE PRESSURE-FLOW RELATIONSHIP

Figure 14 shows a continuous plot of the expected running pressure (P_{run}) versus time, during infiltration at a low flow rate in an adult forearm cannula site. We notice that the pressure level before infiltration is in the 10 to 20 mm Hg range and that a dip in P_{run} occurs as the catheter tip finds its way outside the vein. This is because the pressure in the tissue surrounding the vein is lower than pressure in the vein.[14] If it were not, the tissue would compress and collapse the vein. Simultaneously with the fall in P_F at the time of infiltration, P_0

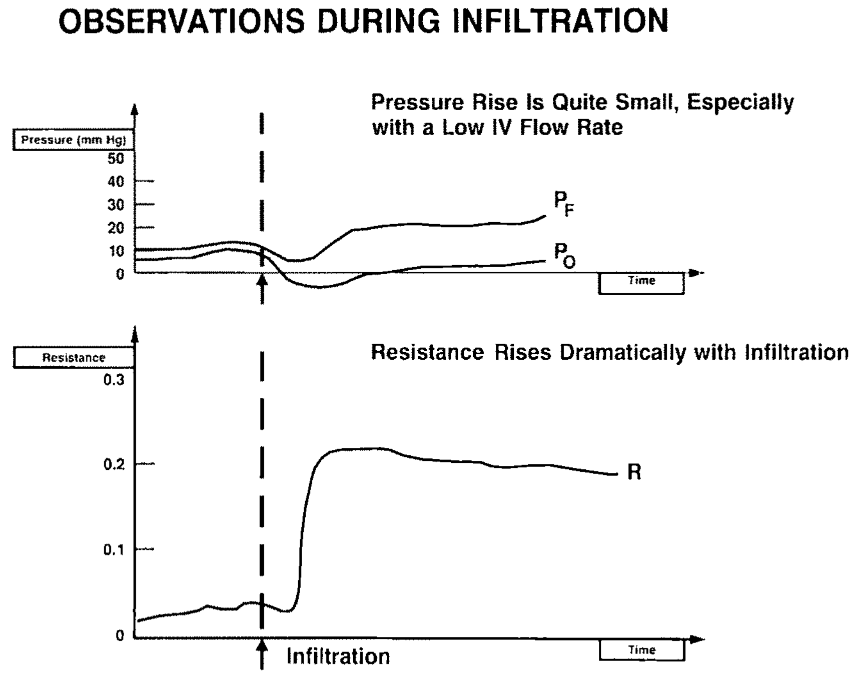


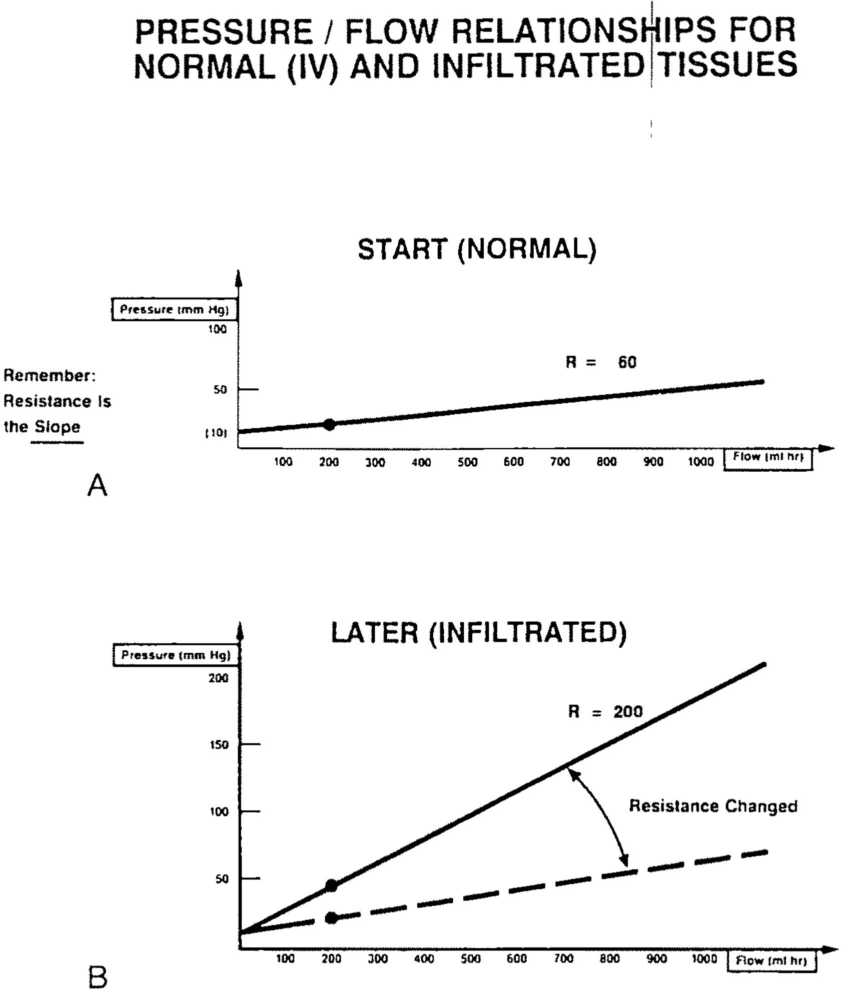
Figure 14. Pressures observed during sudden extravascular movement of an IV catheter.

falls. The fall in P_0 is greater than the fall in P_F, so the resistive pressure, $P_{res} = P_F - P_0$, rises.

As infusate begins to collect in the tissues, a small additional rise in P_{run} may be evident as well as a similar rise in P_{stop} or P_0. It must be noted that at the time of infiltration and for some time thereafter (when not much fluid has yet been infused into tissues), the change in P_{run} is small. This is the limitation of attempting to monitor the IV site by only monitoring pressure.

Following the same time course of events, however, we can see that resistance rises dramatically on infiltration (Fig. 14). This is because $\Delta P = P_{res} = P_F - P_0$ increases while ΔF remains fixed. $R = \Delta P/\Delta F$ thus reflects the rise in ΔP as a rise in resistance. In many patients, the slope of the PFR is changed by a factor of 5 to 20 times when the catheter is extravascular. The large magnitude of this change gives resistance much better promise for detecting infiltration than does pressure rise.

Figure 15 shows the PFR in a normal vein and in an infiltration. Initially, the catheter is located in the vein (15A) and $P_{run} = 22$ mm Hg, $P_{stop} = 10$ mm Hg, $F = 0.2$ L per hour, and $R = 60$ mm Hg per L per hour. Later, the catheter extravasates and P_{run} rises to 50 mm Hg at a flow of 200 ml per hour; $R = 200$. In this case, P_{run} did not exceed even the low level of 50 mm Hg. The feature to note is the difference in slope of the two lines. Such an increase in slope of the PFR appears


PRESSURE / FLOW RELATIONSHIPS FOR NORMAL (IV) AND INFILTRATED TISSUES

START (NORMAL)

LATER (INFILTRATED)

Figure 15. PFR for a normal IV site (*A*) and infiltrated IV site (*B*).

to be *characteristic* of most infiltrations. It is interesting to note that at the low flow rates to the left side of the graph, while the pressure rise would be small, the change in resistance (slope) would be just as large as at higher rates, but because of the low pressure difference involved, it would be more difficult to measure it accurately.

Resistances have been determined for a number of common IV devices and infusion system components (Fig. 16).[14,16,18] Standard bore tubing is noted to have minimal resistance (4 mm Hg per L per hour). It will thus have a minimal effect on the system resistance despite it length. Microbore tubing has a resistance near that of larger bore catheters but still far below that of small bore (high number) catheters. Vein resistance is quite low, as well. On the other hand, resistances noted during infiltration are far above the range of mea-

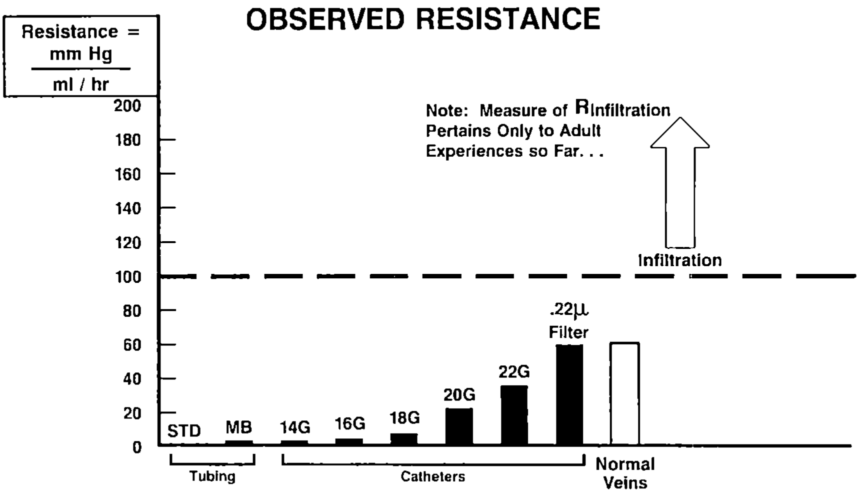


Figure 16. Resistances observed in IV system components and patient veins and tissues.

sured IV system components and veins. In a series of 55 subjects, mean vein resistance was 22 mm Hg per L per hour while mean tissue (infiltration) resistance was 1125 mm Hg per L per hour. Figure 17 shows the distribution of these resistances.[19]

As fluid is infused into extravascular tissues, a rise in P_0 is seen as

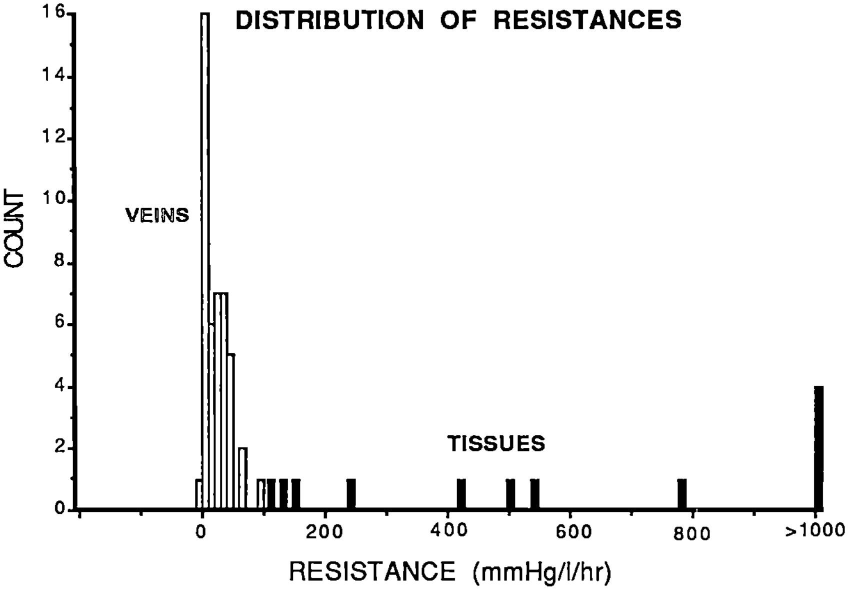


Figure 17. The distribution of vein and tissue resistance from 55 subjects.[19]

fluid accumulates in a relatively confined space. The rise in P_0 is often less than that observed with normal hand elevation.

Much of the data on resistances of IV system components was collected by counting drops, and using a roller clamp and manometer. While this method was cumbersome and crude, it worked. Today portions of this data could be duplicated comparatively quickly using the IVAC Model 560 pump as a test fixture.

OBSTRUCTIONS AND THE PRESSURE-FLOW RELATIONSHIP

It was previously mentioned that $P_{stop} = P_0 = CVP$ when the fluid path (tubing, catheter, and vein) is not obstructed. An obstruction in the fluid path will cause P_0 to rise. A dam (Fig. 18) is a good analogy to help understand this phenomenon.[15]

When the fluid height behind the dam is lower than the top of the dam, no flow occurs downstream. Regardless of the pressure that builds behind the dam, flow remains zero until the fluid level builds to equal and exceed dam height. At that point, flow occurs with negligible resistance. In fact, the quantity of fluid that passes over the dam is only limited by the amount that continues to enter the reservoir above.

Resistance does not increase while the reservoir level rises. The

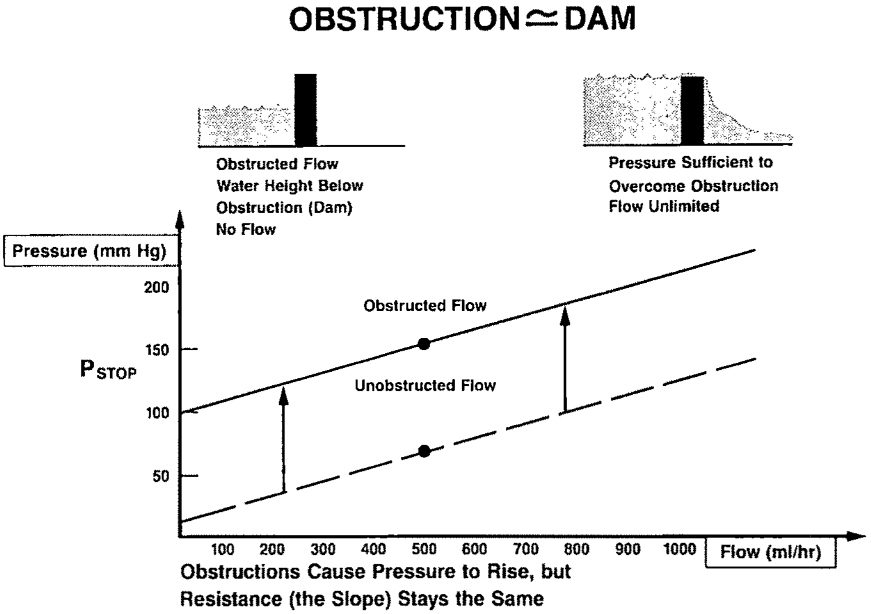


Figure 18. A dam exemplifies obstruction to fluid flow.

dam prevents flow completely, and resistance does not manifest unless there is flow. The dam fully obstructs flow until the fluid pressure rises to equal the height (pressure) of the obstruction. During the filling period, pressure rises despite no flow. This elevation in P_0 is characteristic of an obstruction. The effect on the PFR can be observed in Figure 18 as an upward shift (that is, elevated P_F with no change in slope [resistance, R]).

Vascular obstructions were first described by Knowlton and Starling,[9] who used a collapsible thin-walled rubber tube to produce constant back-pressure (that is, afterload) in his classic studies of heart failure. Although he claimed to control *resistance* with his device, in fact, he produced *constant pressure afterload* with his "Starling resistor." Since that time, collapsible rubber tubes have been studied[2] and reviewed[1,6,23] extensively. The fact that veins collapse completely[5,10,14] makes their behavior quite simple.

A Starling resistor is a conduit that is capable of collapse. Collapse occurs when external pressure (P_{ext}) exceeds internal pressure at the outlet. This occurs under two conditions. If the IV site is elevated above the heart, internal pressure decreases relative to external pressure. Alternatively, if a tourniquet or blood pressure cuff is applied between the catheter and the patient's heart, external pressure increases relative to internal pressure. In either case, flow rate becomes independent of outlet pressure and is determined solely by the difference between inlet pressure and external pressure.[19]

Several common clinical events behave as obstructions (Fig. 19). A partly inflated blood pressure cuff left on a patient's arm applies a pressure that compresses the arm tissues including the veins within. If tissue pressure is 40 mm Hg, the pressure within the veins must rise to equal this value before the veins will be forced open by fluid and flow can resume. In this case, the P_F (that is, P_{run}) measured will be

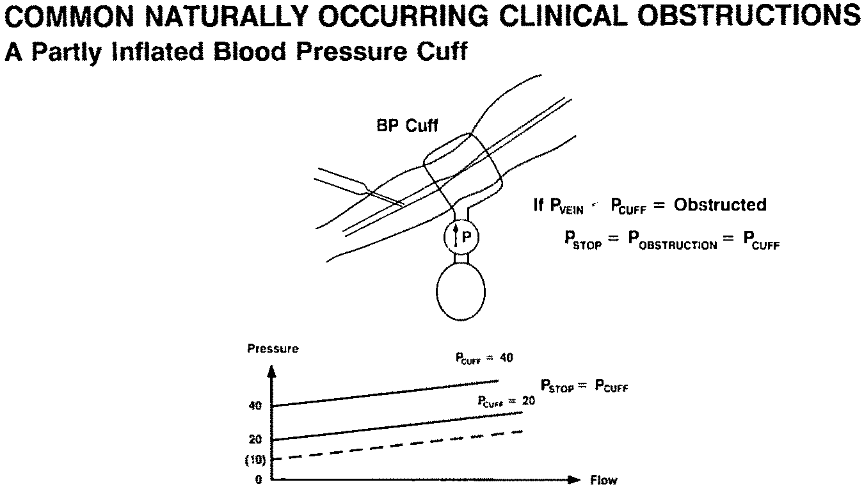

COMMON NATURALLY OCCURRING CLINICAL OBSTRUCTIONS
A Partly Inflated Blood Pressure Cuff
BP Cuff
P
If $P_{VEIN} < P_{CUFF}$ = Obstructed
$P_{STOP} = P_{OBSTRUCTION} = P_{CUFF}$
Pressure
$P_{CUFF} = 40$
$P_{STOP} = P_{CUFF}$
$P_{CUFF} = 20$
40
20
(10)
0
Flow

Figure 19. A partly inflated blood pressure cuff is a common clinical obstruction.

elevated to approximately the cuff pressure. P_0 (that is, P_{stop}) will be elevated to approximately this value as well. P_0 clearly will not equal CVP; rather, it equals P_{cuff} (more generally, P_{ext} or P_{obst}, representing external pressure and obstructing pressure). Despite physical application of a blood pressure cuff, the resistance in the system will be changed little if at all from its low, unobstructed value.[18]

Another common obstruction appears to be the catheter tip against the vein wall (Fig. 20). When this occurs, the tip of the catheter becomes positioned so that the vein wall becomes the obstruction, and the tiny cross-sectional area blocked can easily generate large obstructing pressures of P_{obst} = 70 to 80 mm Hg.

Vein pathology (edematous vein wall, phlebitis, venospasm) can also create an obstruction as pictured, and will cause a corresponding elevation in P_0 (Fig. 20). It is possible that resistance may rise as well.

As a technical note, we must ensure that the pressure measuring device (pump or transducer) is properly aligned with the reference level (right atrium) for P_0 to be interpretable. This alignment problem is eliminated when monitoring resistance, since the hydrostatic error term disappears when the difference between two pressures (ΔP) is computed.

Figure 21 summarizes the PFRs discussed so far. In all four graphs, the PFR describing infusion pressures in the normal vein has a low slope (R) and its intercept with the zero-flow axis (P_0) is central venous pressure (CVP). When the same catheter is located in infiltrated tissues, the resistance (slope) rises dramatically. When the vein, catheter, or tubing become partly obstructed, P_0 rises and resistance remains unchanged.

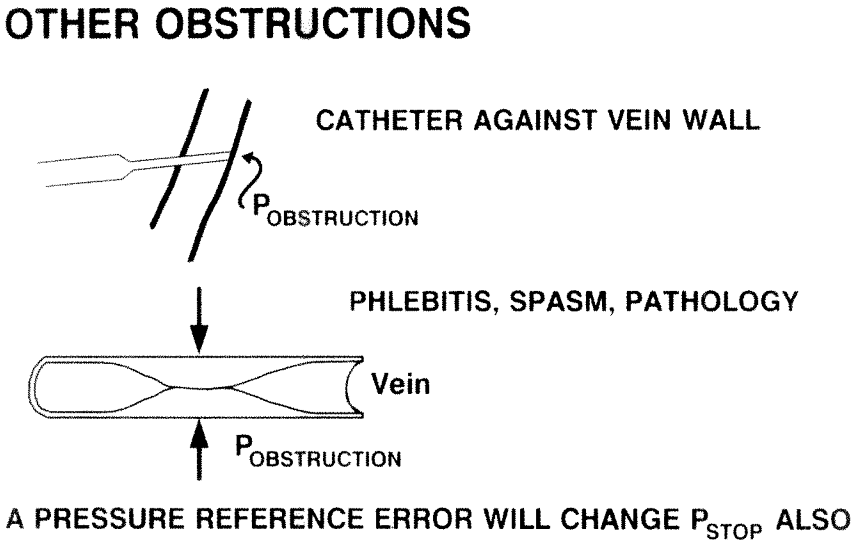

OTHER OBSTRUCTIONS
CATHETER AGAINST VEIN WALL
$P_{OBSTRUCTION}$
PHLEBITIS, SPASM, PATHOLOGY
Vein
$P_{OBSTRUCTION}$
A PRESSURE REFERENCE ERROR WILL CHANGE P_{STOP} ALSO

Figure 20. Other obstructions include catheter against a vein wall, phlebitis, spasm, and other pathology.

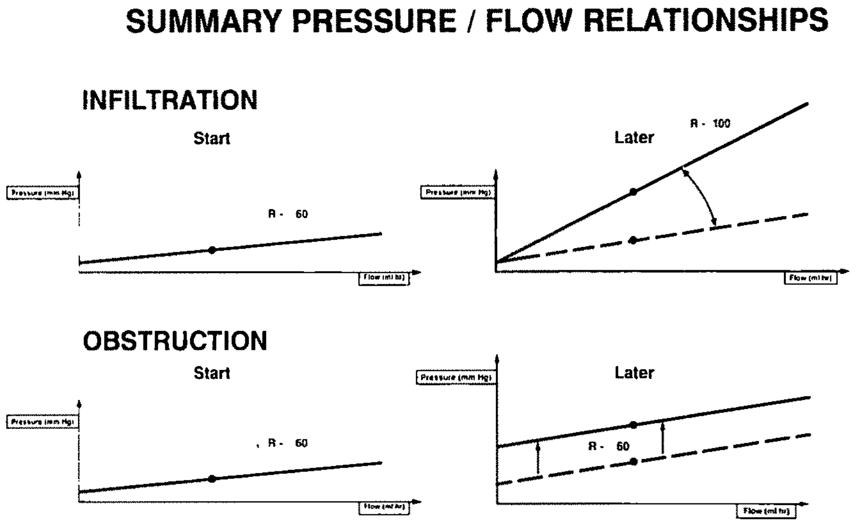


Figure 21. PFR for a normal vein and the complications of infiltration and obstruction.

MONITORING THE INTRAVENOUS SITE WITH COMMERCIALLY AVAILABLE CONTROLLERS AND PUMPS

When either infiltration or obstruction occurs, running pressure displayed (P_{run}) may be elevated. However, P_{run} can have the same value in both clinical conditions. The relationship between P_{run} with obstruction and with infiltration depends on the infusion rate employed (Fig. 21). Obtaining P_{stop} will usually distinguish between the two conditions. If P_{stop} has not changed from its earlier value while P_{run} has risen, we know that the slope of the graph ($R = \Delta P/\Delta F$) had to increase, indicating likely infiltration. But if P_{stop} has risen the same amount as P_{run}, we know the slope of the graph (resistance) has not changed, and obstruction is the likely problem. Obstructed sites may be recovered, while infiltrated sites probably cannot be, and may require immediate treatment.

The chief importance of distinguishing between an obstruction and an infiltration is the intervention that may be indicated. The nurse can often discover a tubing kink hidden under the covers, or manipulate the catheter to relieve an obstruction and recover the IV site. With an infiltration, however, the IV site is almost always lost. In most infiltrations, elevation of the site and application of heat to encourage absorption of the infiltrated fluid is recommended. With infiltration of some potent drugs, injection of neutralizing solutions may be indicated. Rarely (for example, Adriamycin), the tissue into which the drug has extravasated should be removed surgically as soon as discovered to prevent its spread through adjoining tissue and thereby avoid widening necrosis.[4] Both controllers and pumps have the potential to monitor the IV site, as long as they monitor the specific variable they do not control. That is, controllers or pumps that *control flow* must *monitor pressure or resistance,* or preferably both.

AUTOMATIC INTRAVENOUS CONTROLLERS

From the perspective of IV site monitoring, the disadvantage of the controller versus the pump is that the current controllers cannot measure P_0. Without a second F,P pair, it is impossible to calculate resistance or plot the PFR in an effort to distinguish between infiltrations and obstructions. Nonetheless, the pressure-monitoring controller can be a useful tool for IV site protection. Once the controller alarm sounds or the flow status lights indicate a rise in either patient pressure or resistance, visual inspection of the site and circumstances will often lead the nurse or physician to correctly discern whether or not the problem is an infiltrated catheter and extravasated drugs. However, if the problem is not obvious, the flow status indicator may be observed while the catheter is manipulated to see if a positional catheter tip can be identified and relieved. If the flow status indicator cannot be returned to the normal range by manipulating the catheter, most likely the problem is infiltration.

AUTOMATIC INTRAVENOUS PUMPS

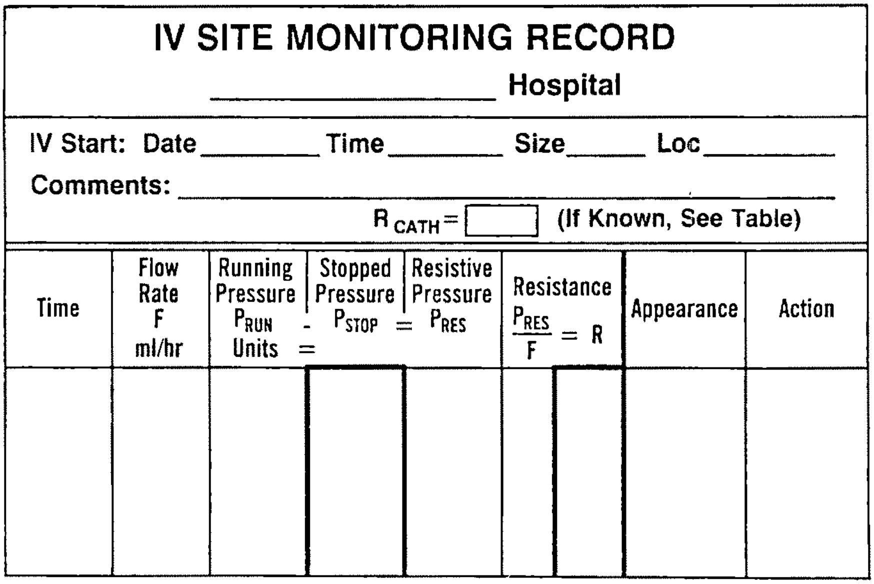
With a pressure monitoring pump (that is, IVAC Model 560), the technique for measuring resistance is simple: start the infusion at the desired flow rate, F; read P_{run}; read P_{stop}; compute $R = (P_{run} - P_{stop})/F$; and use $P_0 = P_{stop}$.

The value for R and P_0 may be obtained each time the IV site is routinely checked or when a patient complains of IV site pain. Tracking these values involves developing a simple written record that additionally assists in the calculations (Fig. 22).

Monitoring R and P_0 during purposeful manipulations of the cannula often provides useful information to assist clinical management. Clearly, automatically computing R each time a button is pressed to stop flow would be a simple but useful feature in a commercial instrument. *Continuous* monitoring of resistance and other variables could follow.

PLACING AVAILABLE TECHNOLOGY IN PERSPECTIVE

Infusion pumps and controllers can be considered on a sliding scale that evaluates their capability to provide site monitoring assistance to the clinician. We have traditionally thought of pumps and controllers as quite different from one another in this regard. Pumps were considered dangerous while controllers were judged safe. This



IV SITE MONITORING RECORD

________________ Hospital

IV Start: Date________ Time________ Size_____ Loc________

Comments: ________________________________

R_{CATH} = ☐ (If Known, See Table)

Time	Flow Rate F ml/hr	Running Pressure P_{RUN} - Units =	Stopped Pressure P_{STOP} =	Resistive Pressure P_{RES}	Resistance $\frac{P_{RES}}{F} = R$	Appearance	Action

Figure 22. IV site monitoring record.

deduction was based on evidence that pumps can force infusate into tissues outside the vein combined with the thought that extravascular tissue would prove sufficient to stop a gravity infusion regulated by an automated controller, and call the nurse to the bedside.

In the late 1970s and early 1980s, most manufacturers lowered pump output pressure limits to an arbitrary 10 or 15 psi from the 25 psi or greater limits of earlier models. This recognized that infusion pumps were being used on peripheral lines and for the infusion of drugs that were potentially necrotic if infiltrated. The pumps had a single, fixed pressure alarm limit, and the response times of the alarms were quite variable. While there was no information to support it, the notion evolved that a 10 psi limit was "safe." In fact, this pressure is many times greater than naturally observed physiologic pressures (Fig. 23). Such pumps can infuse significant volume without alarm, until gross clinical infiltration in finally evident.

More recently, several manufacturers have offered pumps with two or more selectable pressure alarm limits, typically with one in the 4 to 5 psi range and one in the 10 to 15 psi range for clinical situations requiring higher pressure. While advertised as "variable pressure pumps" or "pump/controllers," these products do not all work in the same way or provide the same benefits.

Presumably, one aspect of IV site monitoring is an alarm that calls the nurse to the bedside whenever the (albeit relatively sensitive) alarm limit is exceeded, indicating that a previously running IV has encountered significant resistance or obstructing pressure.

Currently, a pressure-monitoring volumetric pump provides mea-

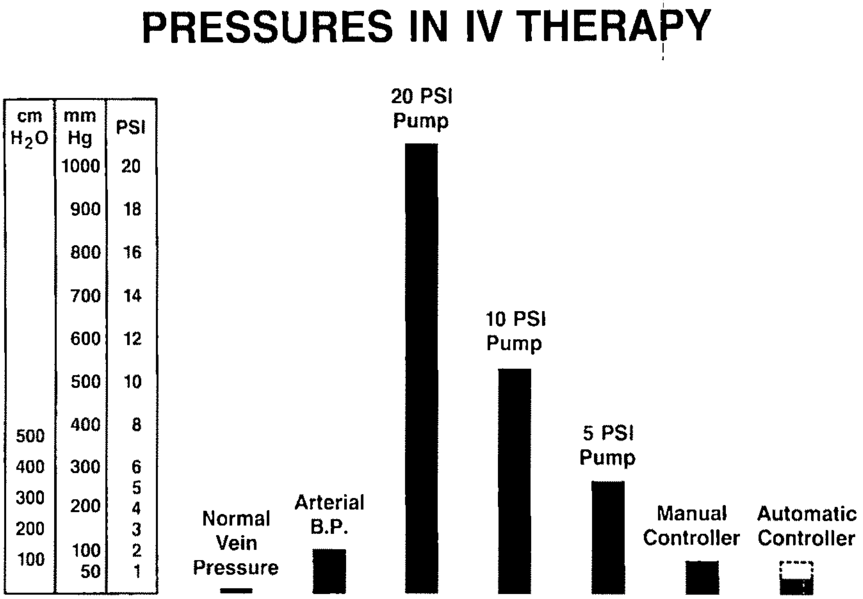


Figure 23. Pressures observed in IV therapy.

surements that offer insight into events at the catheter tip. It does so by providing direct data from which to calculate resistance as a more definite indicator of infiltration or other site problem. This capability provides an enhanced level of IV site monitoring and has the potential to reduce complications of IV therapy.

SUMMARY

This is an exciting time for IV therapy. Use of the IV route of administration continues to increase as patient acuity in today's hospitals increases. IV therapy is not without risks, however, and a fuller understanding of the physical principles employed could help clinicians to reduce the incidence and severity of injuries resulting from drug extravasation (that is, tissue infiltration) and separate this dangerous phenomenon from less serious partial vein obstruction.

This article summarizes a new conceptual model that can be demonstrated and used by making simple measurements during IV therapy. The model and technique employ an infusion pump that measures pressure, allowing the user to manually calculate resistance to fluid flow. Observing a rise in *resistance* at the IV site is an early indicator of undesirable changes at the catheter tip (that is, drug extravasation, catheter infiltration), even before the effect of these changes is visible or palpable on inspection of the IV site.

Using insights obtained from the model, we observe that a properly used pressure-monitoring pump can detect resistance and obstruction to flow and differentiate between them. Also, it appears that suboptimal location of the catheter tip can be detected, and CVP can sometimes be measured from a peripheral IV site.

Requirements for "instrument-assisted IV site monitoring" are (1) a flow source (IV pump), (2) a pressure monitoring system (transducer with pressure readout), and (3) the ability to analyze the PFR. This can be done most simply by measuring pressure at two or more flow rates and calculating P_0 and R, the intercept and slope of the pressure versus flow graph. PFR analysis (computing R and P_0) is subject to electronic software programming and could easily be added to the software of existing pressure-monitoring infusion instruments to provide intermittent IV site evaluation. If R and P_0 monitoring were performed continuously and automatically, infiltration and obstruction could be detected and diagnosed. The quality of IV infusion, protected by site monitoring, would be enhanced significantly. This development could establish a new standard for IV site care.

REFERENCES

1. Caro CG, Pedley TJ, Schroter RC, et al: The mechanics of the circulation. Oxford, Oxford, University Press, 1978, pp 434–512
2. Conrad WA: Pressure-flow relationships in collapsible tubes. IEEE Trans Biomed Instru 16:284–295, 1969
3. Ferenchak P, Collins JJ, Morgan AP: Drop size and rate in parenteral infusion. Surgery 70:674–677, 1971
4. Flack FC, Whyte TD: Behaviour of standard gravity-fed administration sets used for intravenous infusion. Br Med J 3:439–443, 1974
5. Franklin KJ: A Monograph on Veins. Springfield, IL, Charles C Thomas, 1937
6. Fung YC: Biodynamics—circulation. New York, Springer-Verlag, 1984, pp 166–223
7. Hutchinson PM, Yeoman PM, Byrne AJ: Evaluation of the IVAC 560 volumetric pump. Anaesthesia 40:996–999, 1985
8. Kitrenos JG, Jones M, McLeod DC: Comparison of selected intravenous infusion pumps and rate regulators. Am J Hosp Pharm 35:304–310, 1978
9. Knowlton FP, Starling EH: The influence of variations in temperature and blood-pressure on the performance of the isolated mammalian heart. J Physiol (Lond) 206–219, 1912
10. Kresch E, Noordergraaf A: A mathematical model for the pressure-flow relationship in a segment of vein. IEEE Trans Biomed Instru 16:335–338, 1969
11. La Cour D: Drop size in intravenous infusion. Acta Anaesth Scand 24:35–41, 1966
12. Leith DE: Physiological waterfalls. The Physiology Teacher (Am Physiol Soc) 5:6–7, 1976
13. MacCara ME: Extravasation: A hazard of intravenous therapy. Drug Intel Clin Pharm 17:713–717, 1983
14. Moreno AH, Katz AI, Gold LD, et al: Mechanics of distension of dog veins and other very thin-walled tubular structures. Circ Res 27:1069–1080, 1970
15. Permutt S, Riley RL: Hemodynamics of collapsible vessels with tone: The vascular waterfall. J Appl Physiol 924–932, 1963
16. Philip BK, Philip JH: Characterization of flow in intavenous infusion systems. IEEE Trans Biomed Eng 30:702–707, 1983
17. Philip BK, Philip JH: Characterization of flow in intravenous catheters. IEEE Trans Biomed Eng 33:529–531, 1986
18. Philip JH: A model for intravenous fluid administration. IEEE/EMBS 1351–1353, 1987

19. Philip JH: Resistance to fluid flow can detect venous catheter infiltration [abstr]. Anesthesiology 67:A194, 1987
20. Philip JH, Philip BK: Hydrostatic and central venous pressure measurement by IVAC 560 infusion pump. Med Instru 19:232–235, 1985
21. Plumer AL, Cosentino F: Principles and Practice of Intravenous Therapy. Chicago, Scott Foresman, 1987
22. Rapp RP, Rapp DA, Bivins BA, et al: Comparative accuracy of five intravenous-fluid controllers. Am J Hosp Pharm 41:2634–2640
23. Shapiro AH: Steady flow in collapsible tubes. J Biomech Eng: ASME 99:126–147, 1977
24. Upton J, Mulliken JB, Murray JE: Major intravenous extravasation injuries. Am J Surg 137:497–506, 1979
25. Wetmore N: Extravasation—the dreaded complication. Natl IV Ther Assoc 8:47–49, 1985
26. Ziser M, Feezor M, Slolaut MW: Regulating intravenous flow: Controller versus clamps. Am J Hosp Pharm 36:1090–1094, 1979

Department of Anesthesia
Brigham and Women's Hospital
75 Francis Street
Boston, MA 02115

0889–8537/88 $0.00 + .20

The Physiologic Basis of Cardiovascular Monitoring

Rocco Marando, MD, and Alan J. Schwartz, MD, MSEd†*

Anesthesiologists often characterize themselves as clinical pharmacologists to the operating room and intensive care area.[20] Is pharmacologic manipulation really the principal activity of the anesthesiologist? When one reflects on or observes what an anesthesiologist does, the resounding answer is no! Anesthesiologists are clinical physiologists who act as monitors. Before a single drug is administered, a preoperative evaluation is completed. Before induction of the anesthetic state, a baseline set of physiologic measurements are recorded. Before the surgeon is permitted to start the operative procedure and throughout the entire surgical manipulation, maintenance of the anesthetized patient is guided by monitoring that either reaffirms the current anesthetic regimen or prescribes a new one. Anesthetic practice, therefore, allows the fundamental principles of medical practice, namely diagnosis or assessment (monitoring) first, followed by therapy and assessment of therapeutic effect (continued monitoring).

Monitoring of the patient's cardiovascular system is of prime importance to the anesthesiologist. This begins in the preoperative period and continues through the operative, transport, and postoperative phases. Evaluation of *perfusion* is the ultimate aim of cardiovascular monitoring. In its broadest sense, perfusion is the delivery of O_2 to tissues in sufficient quantity to meet metabolic needs and is a reflection of total body O_2 requirements. When monitoring indicates inadequate systemic perfusion, hypoxemia and anaerobic metabolism may be present with resultant acidosis, possibly leading to the clinical state of shock. Shock may be defined as an acute clinical syndrome initiated by hypoperfusion and severe organ dysfunction vital to survival.[14] Perfusion can also be viewed in the context of regional O_2 delivery. Insufficient myocardial O_2 supply, for example, precipitates a cascade of pathophysiologic events for which specific monitoring

---

*Assistant Professor, Department of Anesthesiology, Yale University School of Medicine, Yale-New Haven Hospital, West Haven Veterans Administration, Medical Center, West Haven, Connecticut

†Associate Dean of Academic Affairs, Professor of Anesthesiology, Hahnemann University Hospital, Philadelphia, Pennsylvania

techniques are employed. These may manifest as ischemia (electrocardiogram ST-segment changes), pulmonary vascular congestion (elevated pulmonary capillary wedge pressure), and reduced cardiac output (CO).

Understanding the concept that physiologic cardiovascular monitoring is designed to assess total body and regional organ or tissue perfusion is key to appropriate use of these monitors. It is the authors' intent not to detail every cardiovascular monitor in existence, but rather to explore several monitoring methods so that the reader can understand the physiologic concepts and apply these principles in other situations not described.

MYOCARDIAL MUSCLE MECHANICS

Much of our understanding of cardiac function comes from the study of the isolated papillary muscle preparation (Fig. 1). This experimental apparatus consists of a vertically mounted papillary muscle preparation, the lower end of which is attached to a strain gauge. The upper end is connected to one arm of a lever, with weight attached to the other arm. Resting tension or preload is determined by the amount of weight suspended from the arm. As weight is increased, muscle fiber length and thus preload increases. A vertical stop is then

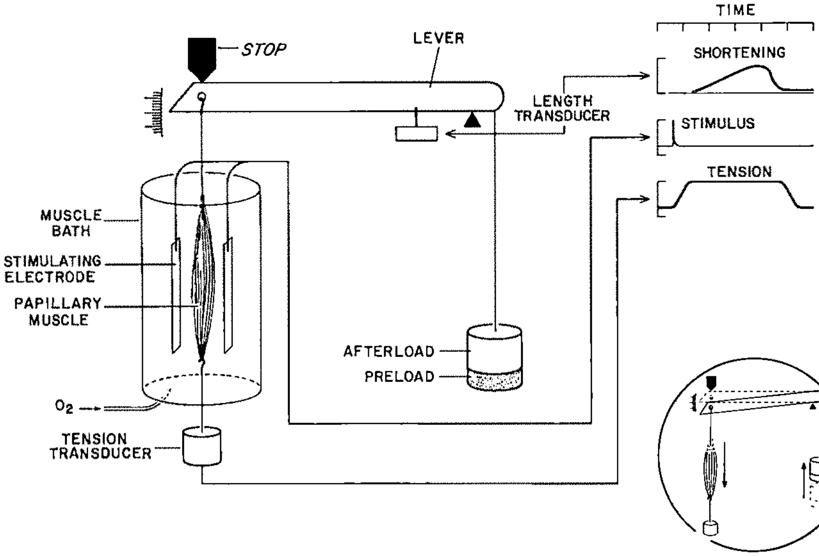


Figure 1. Schematic drawing of isolated papillary muscle preparation. The weight-producing preload stretching force, and the additional weight-producing afterload are shown. The vertically moving stop preventing additional stretch by the afterload weight is shown. (*From* Barash PG, Kopriva CJ: Cardiac pump function and how to monitor it. *In* Thomas SJ [ed]: Manual of Cardiac Anesthesia. New York, Churchill Livingstone, 1984, pp 1–34; with permission.)

placed on the muscle side of the lever so that additional weight may be added to the stack without changing preload. This additional load is not experienced by the muscle until shortening begins and is therefore termed afterload.[15] Determinants of papillary muscle function are analogous to the determinants of myocardial performance in the intact heart.

PHASES OF MYOCARDIAL CONTRACTION

Myocardial contraction may be divided into three distinct phases[1] (Fig. 2):

1. The resting phase occurs prior to muscle stimulation, with the muscle exhibiting a resting length determined by the preload weight.
2. The isometric contraction (constant length) phase begins with muscle stimulation, with tension developing without a concomitant change in muscle length. Developed tension depends on resting myocardial fiber length and contractile plotting length versus active tension allows a length active-tension curve to be constructed.

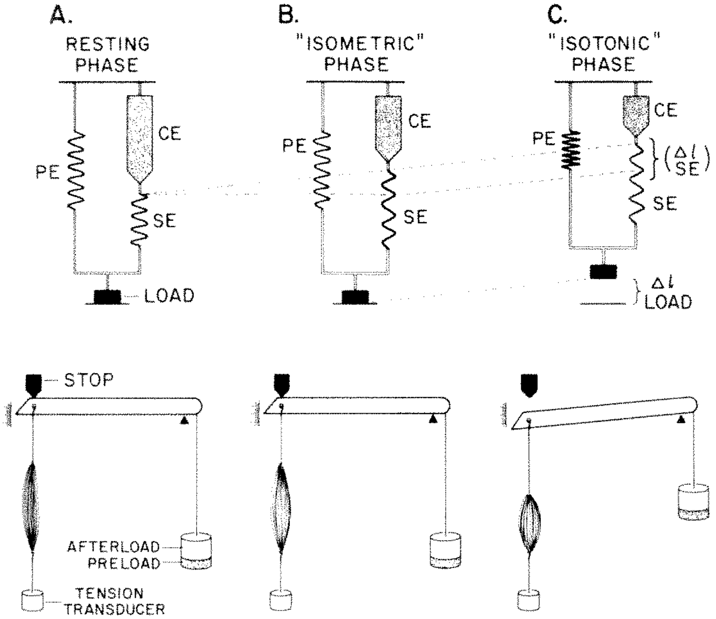


Figure 2. The three phases of myocardial contraction: resting (*A*), isometric (*B*), and isotonic (*C*). *B* is an instant during active isometric contraction and *C* is an instant during afterloaded isotonic contraction. During isotonic contraction SE does not change length and muscle velocity equals CE velocity. Δl = change in length, CE = contractile element, SE = series element, PE = parallel element. (*From* Barash PG, Kopriva CJ: Cardiac pump function and how to monitor it. *In* Thomas SJ (ed): Manual of Cardiac Anesthesia. New York, Churchill Livingstone, 1984, pp 1–34 ; with permission.)

3. In the isotonic contraction (constant tension) phase, muscle shortening occurs at a constant developed muscle tension equal to the sum of preload and afterload. Isotonic contractions require four variables to define mechanical function: force (tension), instantaneous length, time after activation, and shortening velocity (rate).

Contractility Models

Hill (1938) working with skeletal muscle, proposed the active state model for studying the contraction process. This model was composed of two elements: the contractile element (CE) and the series elastic element (SE). Basic differences exist between skeletal and cardiac muscle, including resting tension and transition from resting state to full contractile activity,[15] that make applicability of this model to myocardial cells difficult. In an attempt to describe myocardial contractility two additional models have been proposed, the Maxwell and Voight models. These have added a third or parallel elastic element (PE), either in parallel (Maxwell) or in series (Voight) with the series element. In the preferred muscle model for estimating total cardiac muscle elasticity, that by Maxwell, the contractile element manifests its force externally by shortening against a passive series elastic element. During isometric contractions, stretch of the SE allows the CE to develop its maximum force without changing muscle length. During isotonic contraction the CE develops tension while the length of the SE remains constant. Thus, muscle velocity equals contractile element velocity. The PE, in parallel with the SE, accounts for the significant resting tension found in cardiac muscle. The PE is probably connective tissue, acting to prevent overstretch of cardiac muscle during diastole.

Force Velocity Curve

Understanding the contractility model allows one to construct a force-velocity curve, perhaps the gold standard for characterizing myocardial function. The papillary muscle preparation may be used to construct such a curve. The curve is generated by plotting weight against shortening velocity. For each weight or load, two curves may be constructed: one describing the force (tension) time course and the other the length (shortening) time course (Fig. 3). Thus, the resting muscle tension and the rate of rise and peak tension measured on stimulation of the muscle are all greater when the weight stretches the muscle as compared with the unstretched muscle. However, the time to peak tension is unchanged. As the initial muscle length is stretched by the *preload*, the work of the muscle is increased.

MONITORING THE HEART AS A PUMP

The prime function of the heart is to pump oxygenated blood in sufficient quantity to meet the body's metabolic demands. Adequate

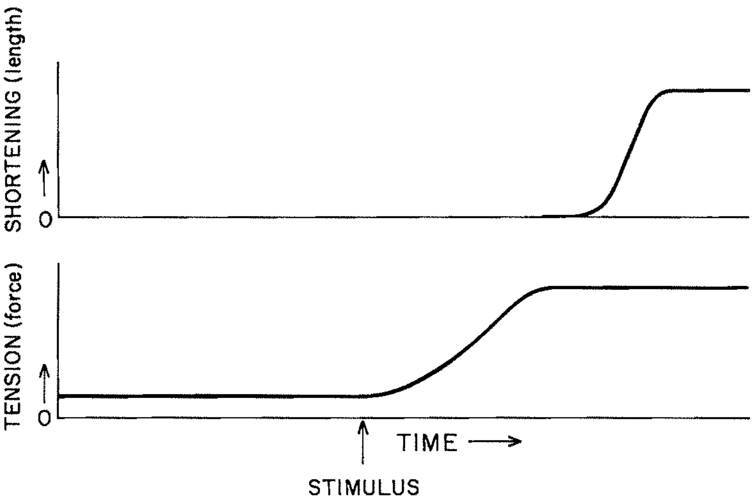


Figure 3. Simultaneous recording of tension and shortening for a contraction against an afterload. Tension development begins after onset of stimulation once tension equals load shortening begins a maximal rate amount of muscle shortening equals distance the load is moved. (*From* Barash PG, Kopriva CJ: Cardiac pump function and how to monitor it. *In* Thomas SJ (ed): Manual of Cardiac Anesthesia. New York, Churchill Livingstone, 1984, pp 1–34; with permission.)

pumping function depends on rhythmic, synchronized, and forceful contraction of the cardiac muscle. Put into physiologic terms, the pumping function of the heart depends on (1) heart rate, (2) preload, (3) afterload, and (4) contractility.

Heart Rate

Heart rate defines the number of times per minute the heart contracts. Heart rate is under intrinsic, as well as neural and humoral control. Half a century ago, Rosenblueth and Simeone[12] performed quantitative studies of cardiac parasympathetic-sympathetic interactions. Normally, sinus node pacemaker cells initiate cardiac activation. An action potential is generated and conducted to atrial myocardium across the atrioventricular node, through the bundle of His, bundle branches, and Purkinje fibers and into ventricular myocardium. It is known that sinoatrial nodal tissue is usually under the tonic influence of both the sympathetic and parasympathetic divisions of the autonomic nervous system. That these two systems interact has been shown by Levy.[7] He found that the heart's response to a given level of vagal stimulation varied substantially with the existent level of sympathetic activity. Normal resting individuals have a low tonic level of sympathetic activity. Sympathetic nervous system activity enhances myocardial performance. This is mediated via norepinephrine and other catecholamines that interact with cardiac cell membrane beta adrenergic receptors. This interaction activates adenylate cyclase, which leads to elevated levels of cyclic AMP intracellularly.

This second messenger activates protein kinases, causing protein phosphorylation and releases of calcium. Intracellular calcium is released and binds to the protein troponin. This complex then interacts with tropomyosin allowing actin and myosin to crosslink, ultimately leading to myofibril contraction and tension development.[2]

Heart rate is a primary determinant of both myocardial O_2 demand and supply. Myocardial O_2 consumption is directly dependent on heart rate. In the left ventricle, the greatest proportion of coronary blood flow occurs during diastole. In the subendocardial region the majority of flow occurs during diastole. Therefore, subendocardial blood flow is particularly vulnerable to the shortened diastolic period associated with tachycardia. Normally, myocardial O_2 demand and supply are closely matched. Myocardial ischemia develops as a result of an imbalance between O_2 supply and consumption at the cellular level. Monitoring electrical events via electrocardiography may detect ischemia manifesting as ST-segment and T-wave changes.

Effective forward CO depends on coordinated pumping of the atria and ventricles. Loss of the atrial contribution ("atrial kick") to ventricular filling can result in a 20 per cent or greater decrease in CO. EKG monitoring indicates the loss of atrial contribution by the absence of P waves, providing an explanation for decreases in BP and CO. Dysrhythmias may impact on perfusion by disrupting the normally coordinated contraction sequence between atria and ventricles. When the atria and ventricles contract independently of each other, the ventricles filling may decrease, also leading to decreases in CO. ECG monitoring indicates the presence of a dysrhythmia, and correlated with hemodynamic monitoring, indicates the clinical significance of the electrical disturbance.

Preload

Otto Frank (1895) and Ernest Starling (1914) contributed to our understanding of perfusion by describing the relationship between ventricular end-diastolic volume and CO. A direct relationship exists between these two variables within the normal range of ventricular volume and stretch of ventricular muscle. Given constant heart rate, afterload, and contractility, Starling observed that an increase in ventricular volume or preload resulted in CO.[10]

In his Linacre lecture on the "Law of the Heart" delivered in 1915, Starling stated that "the law of the heart" is the same as the law of muscle tissue generally, that the energy of contraction, however measured, is a function of the length of the muscle fibers prior to contraction.[16]

In the intact heart, preload may be defined as the end-diastolic myocardial fiber length prior to contraction. The preload "weight" or stretch of the cardiac muscle is equivalent to ventricular end-diastolic volume. Ideally, cardiovascular monitoring should measure ventricular volume. In the cardiac catheterization laboratory, ventricular volume can be measured using contrast angiography. Such measurements are merely "snapshots" of ventricular filling at one point in time and are not suited to continually monitoring ventricular volume. During the perioperative period, however, hemodynamics change frequently, requiring continual ventricular volume monitoring. In this situation, pressure estimates of preload are the measurements used most often.

One example of a pressure estimate of ventricular filling is the measurement of pulmonary capillary wedge pressure (PCWP) with the pulmonary artery catheter.[18] The basis for pulmonary artery catheter monitoring is twofold. First, during diastole with the mitral valve open, the left ventricular chamber is in open communication with the left atrium. The left atrial pressure is accurately measured by transducing the pressure distal to the catheter tip, with the inflated balloon occluding pulmonary artery blood flow (PCWP). Second, within the clinical range of ventricular volumes (in the absence of myocardial ischemia), as preloaded or filling volume increases, ventricular cavitary pressure increases in almost linear fashion. The inference, therefore, is that a measured increase in PCWP is indictative of an increase in left ventricular end-diastolic pressure (LVEDP), which is in turn indicative of an increase in left ventricular end-diastolic volume (LVEDV). These relationships are valid provided that ventricular compliance is constant, mitral valve function is normal, and that airway pressure is not elevated.

Afterload

In the intact heart, afterload may be defined as the external factors that oppose muscle fiber shortening.[9] As afterload increases, muscle tension must increase in order to achieve shortening, and in the intact heart, ejection of blood from the intact ventricle. Clinically, afterload is the force resisting muscle shortening during myocardial contraction. Afterload is determined by factors related to the peripheral circulation and to the ventricular chamber itself. The latter is described by the law of LaPlace:

$$T = \frac{P\,r}{2h}$$

when T is ventricular wall tension, P is chamber pressure, r represents radius, and h represents wall thickness. Afterload is closely linked to aortic impedance, the sum of external factors opposing ventricular ejection. It may be expressed as a ratio of aortic pressure to flow. As aortic impedance is increased, for example, elevated blood pressure, or increased blood viscosity, left ventricular afterload is increased and stroke volume declines.[4] Afterload is assessed by measurement of BP or by calculation of systemic vascular resistance (SVR) as derived from measurement of CO. Measuring a patient's blood pressure is a mainstay of circulatory monitoring during anesthesia or in the intensive care setting. When first proposed by Cushing, however, the implied value of BP monitoring was as an indicator of the

CO. When it is important to assess peripheral or pulmonary vascular resistances, CO can be measured by a variety of methods, and resistance derived mathematically. Why is it necessary to monitor both afterload and preload? The hemodynamic (pumping) work of the cardiac muscle is directly related to the "loads" placed on it. Additionally, both afterload and preload are determinants of myocardial oxygen demand.[8] In order to appreciate this concept, two hypothetical situations may be considered as they relate to the wall tension and external work contributions to myocardial oxygen demand.

For the first situation, imagine a heart of normal adult size, which contains a given left ventricular volume. The heart is pumping against an outflow pressure (resistance). The volume within the heart is then doubled while the outflow pressure remains constant. This heart will consume more O_2 as it ejects a greater volume. In the second example, imagine again a heart of normal adult size containing a given left ventricular volume and pumping against a constant pressure. This heart is now subjected to a 50 per cent increase in outflow pressure while the left ventricular volume remains constant. Again, this left ventricle will consume more O_2 as it contracts against greater pressure.

Contractility

The fourth and final determinant of ventricular performance is contractility. The definition of contractility has been the subject of a great deal of research and debate. It may be defined as the ability of muscle to develop increased tension independent of loading conditions. Contractility is a fundamental property of cardiac muscle and is dependent on the degree of actin-myosin crossbridge formation.[9] A number of indices and measurements have been proposed for quantifying myocardial contractility. These may be divided into isovolumetric phase and ejection phase indices.[4] Isovolumetric phase indices include the maximum velocity of shortening of unloaded contractile elements (V_{max}) and peak rate of rise of ventricular pressure (maximum dP/dt), while ejection phase indices include ejection fraction, fractional shortening of ventricular myocardium (FS), and velocity of circumferential fiber shortening (V_{cf}) at peak wall stress. Isovolumetric indices are of little value in determining basal contractility levels. However, they are useful in determining acute directional changes.[4] V_{max} appears not to be affected by preload or afterload but is sensitive to inotropic stimuli.[5] Maximum dP/dt as a measure of contractility is based on the view that a fundamental property of contracting myocardium is the rate at which ventricular pressure is developed. Maximum dP/dt may be affected by increases in preload, afterload, and heart rate.[6]

Ejection fraction is defined as stroke volume divided by end-diastolic volume.[11] While frequently useful, the ejection fraction value may be affected by several factors other than contractility. For example, afterload and less often preload may affect ejection fraction. However, the ejection phase indices may be helpful in assessing basal contractility.[4] Fractional shortening, a correlate of ejection fraction, is a comparison between a dimensional change of the left ventricle during systole and its diastolic value.[19] Mean velocity of circumferential fiber shortening is derived noninvasively. It incorporates a time dimension and as such may be more sensitive than the ejection fraction in detecting contractility changes.

PRESSURE-VOLUME RELATIONSHIP

Conceptually, left ventricular performance may be examined by constructing a pressure-volume loop.[2] Such pressure-volume loops relate ventricular chamber size to instantaneous intracavitary ventricular pressures measured throughout the cardiac cycle. To quantify ventricular chamber dimensions, angiography, echocardiography, radionuclide ventriculography, gated computerized tomographic scanning, and magnetic resonance imaging may be employed.[17] No time element is plotted in the loop. Four phases make up the cardiac cycle (Fig. 4). Phase I is that of diastolic filling and takes place from point D to A. A slight decrease in ventricular pressure occurs and is due to ventricular relaxation and distensibility. Closer to point A there is an

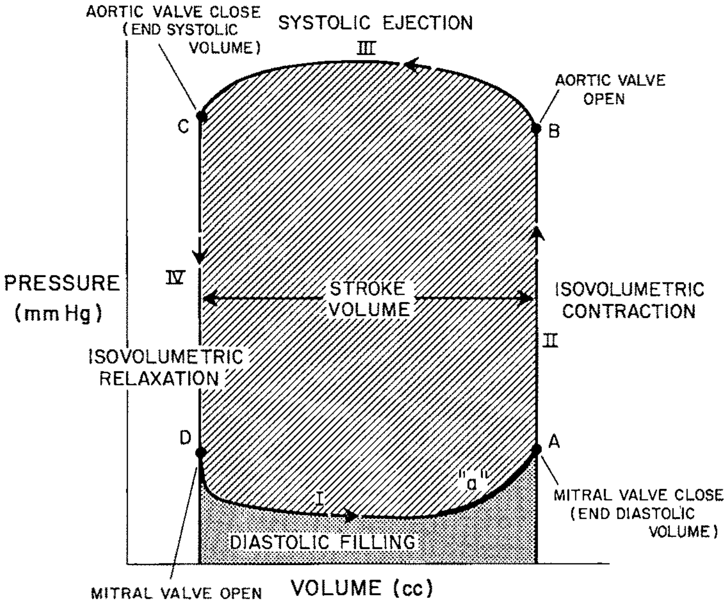


Figure 4. Pressure-volume loop of the left ventricle for one cardiac cycle (D A B C). Note the slight decrease in ventricular pressure occurring in phase I owing to ventricular relaxation and distensibility. Stroke volume is the difference between ventricular volume at end-diastole and end-systole. (*From* Barash PG, Kopriva CJ: Cardiac pump function and how to monitor it. *In* Thomas SJ (ed): Manual of Cardiac Anesthesia. New York, Churchill Livingstone, 1984, pp 1–34; with permission.)

increase in ventricular pressure as ventricular filling continues. This gives the final LVEDP and LVEDV. At point A the mitral valve closes. Phase II, from point A to B, is the period of isovolumic contraction. A significant pressure increase occurs with no concomitant rise in volume. This phase corresponds to isometric contraction in the isolated papillary muscle preparation. At point B the aortic valve opens. Phase III represents systolic ejection, with both rapid and reduced ejection components as one proceeds from point B to C. This phase is similar to isotonic contraction of the papillary muscle preparation, but is said to be auxotonic,[1] the difference being that ventricular contraction occurs against a *varying* afterload as opposed to the constant afterload of an isotonic contraction. At the end of this phase the aortic valve closes. The fourth and final phase is isovolumic relaxation, during which a pressure drop occurs unaccompanied by a volume change. The mitral valve opens at the end of this phase, completing the cardiac cycle.

Analysis of the boundaries of the pressure-volume loop provides insight into left ventricular pump function and work performed. The area within the pressure-volume loop is the stroke work of the ventricle. On the volume axis the loop's width represents stroke volume, or end-diastolic minus end-systolic volume. On the ordinate, the loop's height represents its pulse pressure minus mean left ventricular diastolic pressure minus mean left ventricular systolic pressure. It is possible to use pressure-volume loops obtained at different preloads and afterloads to describe the contractile state of the ventricle. Suga et al and Sagawa,[13,17] using a canine model described the isovolumic pressure line, made by connecting end-systolic points of loops made at different preloads and afterloads. End-systolic fiber length varies inversely with afterload. In the intact heart a relationship exists between end-systolic volume and end-systolic pressure, the former varying inversely and the latter, directly with contractility. The slope of the line relating end-systolic volume to end-systolic pressure defines contractility[4] (Fig. 5). The end-systolic pressure-volume relation may help differentiate poorly contracting ventricles from nor-

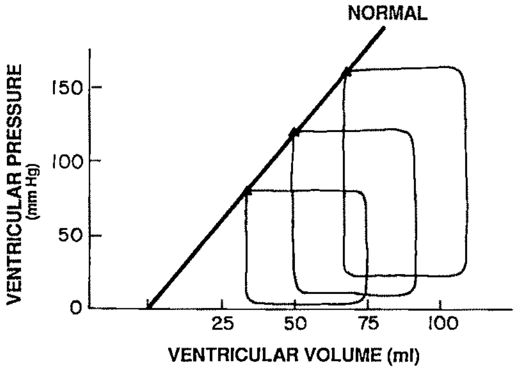


Figure 5. Schematic diagram for the end-systolic pressure-volume relation (ESPVR). Three pressure-volume loops are constructed. The ESPVR relation shows normal contractility. A shift to the left is augmented contractility. A shift to the right of the ESPVR indicates decreased contractility.

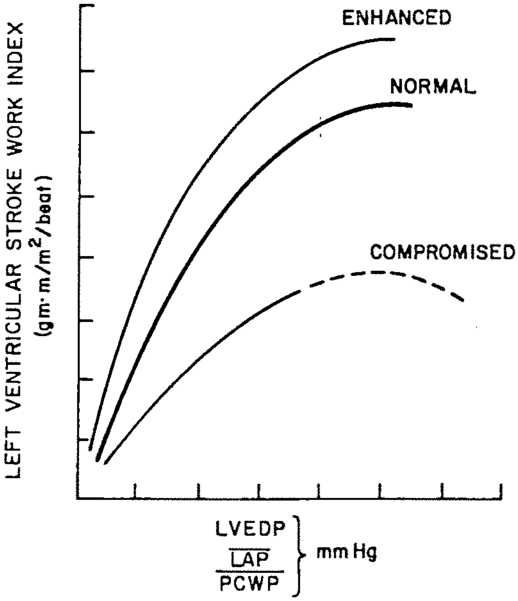


Figure 6. Ventricular function curves illustrating normal, enhanced, and comprised contractility. LVEDP = left ventricular end-diastolic pressure, LAP = mean left atrial pressure, PCWP = mean pulmonary capillary wedge pressure. (*From* Barash PG, Kopriva CJ: Cardiac pump function and how to monitor it. *In* Thomas SJ (ed): Manual of Cardiac Anesthesia. New York, Churchill Livingstone, 1984, pp 1–34; with permission.)

mally contracting ventricles better than can the measure of ejection fraction.

A clinically useful measure of left ventricular function is the ventricular function curve, using the Frank-Starling mechanism[3] (Fig. 6). This curve may be constructed by plotting an index of ventricular performance (for example, CO stroke volume, stroke work, and so forth) on the ordinate and one of myocardial fiber length on the abscissa (LVEDP or PCWP). Owing to the difficulty in directly measuring myocardial fiber length pressure, substitutions are used. This assumes that ventricular pressure and volume are directly proportional. However, the relationship between pressure and volume may not be linear (for example, during episodes of myocardial ischemia). Ventricular function curves for any given patient are constructed by carefully altering blood volume or vascular volume and recording changes in left ventricular filling pressure (for example, PCWP or LVEDP).

As physiologists, anesthesiologists must have an understanding of the basic science of cardiac muscle structure and function. As clinicians we must use the basic science as foundations of cardiac performance to understand the applications and limitations of our monitoring devices.

REFERENCES

1. Barash PG, Kopriva CJ: Cardiac pump function and how to monitor it. *In* Thomas SJ (ed): Manual of Cardiac Anesthesia. New York, Churchill Livingstone, 1984, pp 1–34

2. Berne RM, Levy MN: Cardiovascular Physiology. St. Louis, Mosby, 1986, pp 50–75
3. Berne RM, Levy MN: Cardiovascular Physiology. St. Louis, Mosby, 1986, pp 76–104
4. Braunwald E: Assessment of Cardiac Function in Heart Disease, A Textbook of Cardiovascular Medicine. Philadelphia, Saunders, 1987, pp 449–470
5. Burns JW, Covell JW, Ross J: Mechanics of isotonic left ventricular contractions. Am J Physiol 224:725, 1973
6. Gleason WL, Braunwald E: Studies on the first derivative of the ventricular pressure pulse in man. J Clin Invest 41:80, 1962
7. Levy MN: Cardiac sympathetic-parasympathetic interactions. Fed Proc 43:2598, 1984
8. Lowenstein E: Anesthetic considerations in coronary-artery disease. Refresher Courses in Anesthesiology. 4:51, 1976
9. Milnor WR: Arterial impedance as ventricular afterload. Circ Res 36:565, 1975
10. Patterson SW, Starling EH: On the mechanical factors which determine the output of the ventricles. J Physiol 48:357, 1914
11. Parmley WW: Ventricular function: *In* Parmley WW, Chatterjee K (eds): Cardiology, Vol 1. Philadelphia, Lippincott, 1987, pp 1–20
12. Rosenblueth A, Simeone FA: The interrelations of vagal and accelerator effects on the cardiac rate. Am J Physiol 110:42, 1934
13. Sagawa K: Editorial: The end-systolic pressure-volume relation of the ventricle: Definition, modifications and clinical use. Circulation 63:1223, 1981
14. Schuster DP, Lefrak SS: *In* Civetta JM, Taylor RW, Kirby RR (eds): Critical Care. Philadelphia, Lippincott, 1988, pp 891–908
15. Smith NT: Myocardial function and anesthesia. *In* Prys-Robers (ed): The Circulation of Anaesthesia. Oxford, Blackwell Scientific Publications, 1980, pp 57–114
16. Starling EH: The Linacre Lecture on the Law of the Heart, Cambridge, 1915. London, Longmans, Green, 1918
17. Suga H, Sagawa K, Shoukas AA: Load independence of the instantaneous pressure-volume ratio of the canine left ventricle and effects of epinephrine and heart rate on the ratio. Circ Res 32:314, 1973
18. Swan HJC, Ganz W, Forrester J, et al: Catheterization of the heart in man with use of a flow-directed balloon-tipped catheter. N Engl J Med 283:447, 1970
19. Thys DM, Hillel Z, Goldman ME, et al: A comparison of hemodynamic indices derived by invasive monitoring and two-dimensional echocardiography. Anesthesiology 67:630, 1987
20. Woodbridge P: Changing Concepts Concerning Depths of Anesthesia. Anesthesiology 18:536, 1957

Department of Anesthesiology
Yale University School of Medicine
P.O. Box 3333
New Haven, CT 06510

0889–8537/88 $0.00 + .20

Electrocardiography

Gerard F. McCloskey, MB, BCh, and*
Patrick E. Curling, MD†

It has been 30 years since the electrocardiogram (ECG) began to achieve acceptance as an essential component of the anesthesiologist's monitoring armamentarium. As early as 1960, a description of intraoperative ECG monitoring by Canard and Dripps stated, "Its value is unquestioned but it requires careful interpretation on the part of [the] anesthetist. . . ."[4] The authors cautioned that intraoperative ECG monitoring has its unique limitations based on the operating room environment and the dynamic condition of the anesthetized patient. In modern anesthetic practice, continuous intraoperative ECG monitoring is ubiquitous and essential. Although the initial use of intraoperative ECG monitoring was primarily concerned with the detection of dysrhythmias, its present role has been expanded. Now, with proper use of a calibrated electrocardiogram in conjunction with an appropriate lead system, the anesthesiologist may also diagnose myocardial ischemia, electrolyte abnormalities, and assess pacemaker function. Presently, the evolution of this monitoring modality continues with recent advances in computer-assisted dysrythmia algorithms, ST-trend analysis, intraoperative telemetry, and Holter monitor applications.

LEAD SYSTEMS

In order for the data derived from the electrocardiogram to be clinically useful, the anesthesiologist must observe standard lead system conventions. To accurately diagnose ischemia, the ECG output must be calibrated so that 1 mV deflection measures 10 mm on the strip chart recorder with paper speed adjusted to 25 mm $\cdot$ sec^{-1}. Electronic filtering of the ECG signal, done routinely to minimize artifact and

---

*Assistant Professor, Department of Anesthesiology, Yale University School of Medicine, Yale-New Haven Hospital, New Haven, Connecticut

†Associate Professor, Department of Anesthesiology, Yale University School of Medicine, Yale-New Haven Hospital, New Haven, Connecticut, and Department of Anesthesiology, Emory University School of Medicine, Atlanta, Georgia

interference, must have a low pass threshold of 0.1 Hz (diagnostic mode) to avoid filtering of low-frequency components of the ECG waveform with subsequent distortion of the ST segment. Clinically, this may result in apparent displacement of the ST segment from the isoelectric line simulating ischemia when none actually exists (Fig. 1). More importantly, it may also displace elevated or depressed ST segments toward isoelectric precluding diagnosis of actual ischemia. Some ECG monitors have 4 Hz low pass filters available in "monitor" mode. In this mode, motion and respiratory artifact are minimized, but important information in the ST segments may be grossly distorted.

Intraoperatively, the configuration of the ECG lead system is of extreme importance because it dictates the perspective from which the electrical activity of the heart is viewed. The body functions electrically as a volume conductor and as such, myocardial electrical activity can be obtained anywhere on its surface. Einthoven maintained that in the frontal plane, the heart within the thorax could be represented as an equilateral triangle with the heart at its center. Therefore, an electrode system evolved consisting of three electrodes, one at each angle of the triangle (Einthoven's triangle). These bipolar leads are known as the "standard" limb leads: I, II, and III.[15] To increase the amount of information available in the frontal plane, Wilson developed a system of unipolar leads. This system uses three electrodes in the same positions as the standard leads. However, all three leads are interconnected via a high impedence circuit (5000 Ω) and act as an indifferent or negative electrode at zero potential. One of the three leads is connected to this zero potential as an exploring or positive electrode so that the actual potential difference is measured.[16] Goldberger modified this system by omitting the high impedence circuit

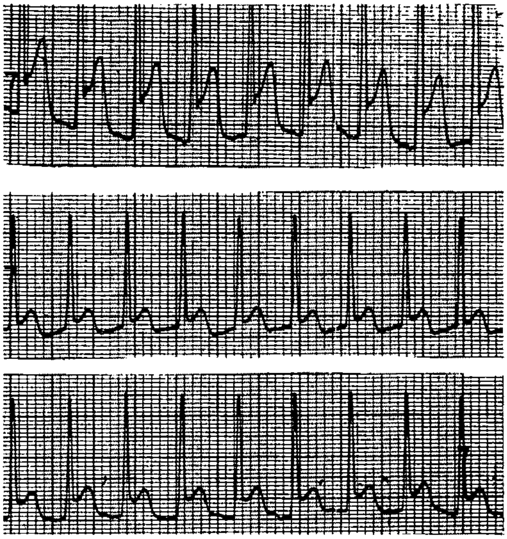


Figure 1. A noncalibrated ECG (*top*) artifactually depicts 9 mm ST-segment elevation. The calibrated middle and bottom traces are filtered from 0.5 to 50 Hz and 0.05 to 100 Hz, respectively. The bottom trace is correctly filtered for ECG diagnosis of ST-segment changes and reveals a 4 mm elevation. (*From* Zaidan JR: Electrocardiography. *In* Barash PG, Cullen B, Stoelting RK (eds): Clinical Anesthesiology. Philadelphia, Lippincott, 1989, pp 587–623; with permission.)

and disconnecting the exploring electrode from the indifferent electrode. This resulted in a unipolar lead system that produced larger or augmented deflections.[7]

When used together, the standard limb leads (I, II, III) and the augmented leads (aVR, aVL, aVF) allow six separate and distinct views of the heart in the frontal plane. Monitoring of cardiac electrical activity in the horizontal plane is achieved by using a series of unipolar precordial leads at standard positions (for example, V_1 to V_6).

Use of the standard 12-lead ECG intraoperatively is impractical. Even a five-lead system capable of monitoring seven leads (I, II, III, aVR, aVL, aVF, V5) may not be present in some operating rooms and intensive care units. However, it is possible to modify the standard lead configurations for specific purposes of either improved dysrythmia monitoring or increasingly sensitive ischemia detection (Fig. 2).

Probably the most commonly modified bipolar lead is MCL_1. In this three-lead system, the left arm electrode is placed in the left subclavicular position, the left leg electrode in the V_1 position (fourth intercostal space to the right of the sternum), and the right arm is used as a ground. The patient is then monitored in the standard lead III position. This facilitates recognition of the P waves, QRS complex, and is useful for detection of dysrythmias and conduction defects.

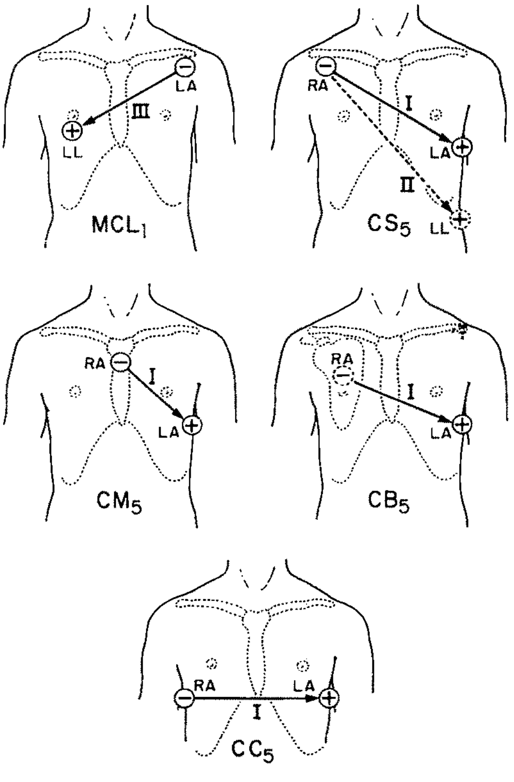


Figure 2. Modified bipolar standard limb lead systems including MCL_1 (modified chest lead), CS_5 (central subclavicular), CM_5 (central manubrium), CB_5 (central back), and CC_5 (central chest). (*From* Griffin RM, Kaplan JA: ECG lead systems. *In* Thys DM, Kaplan JA (eds): The ECG in Anesthesia and Critical Care. New York, Churchill Livingstone, 1987; with permission.)

Another modified bipolar lead is the CS_5 lead. To monitor this lead configuration, the right arm lead is placed in the right subclavicular area, the left arm lead in the V_5 position (fourth intercostal space at the anterior axillary line), and the left leg electrode in its usual position. With the electrocardiogram set on lead I, CS_5 is monitored, which gives a good view of the anterior and lateral walls of the left ventricle and is useful in the diagnosis of ischemia in these areas. Another advantage of this configuration is that switching to monitor lead II actually yields standard lead II and monitors the inferior wall for ischemia.

CM_5 is a third lead system that yields information similar to the CS_5 configuration. The only major difference is that the right arm electrode is moved from a subclavicular location as in CS_5 to a position overlying the manubrium. This allows surgical preparation of the right arm, shoulder, and chest. Lead I is monitored. In a comparison study of various bipolar lead systems, CM_5 was found to detect 63.6 per cent of ST-segment shifts, whereas CS_5 detected only 31.6 per cent.[5]

CC_5 employs the right arm electrode in the fourth intercostal space on the right and the left arm electrode in a similar position on the left. Here too, lead I must be monitored, and is also primarily a configuration for monitoring left ventricular ischemia.

Finally, a modification of a lead system allows for both ischemia detection and improved dysrythmia detection. This system, CB_5, uses the right arm electrode over the right scapula and the left arm electrode on the V_5 position. Again, the monitor is set to the lead I position for detection of ventricular ischemia and standard lead II is used to evaluate dysrythmias.

The previous discussion focused on surface electrode systems. However, it is possible to obtain useful and often essential diagnostic information from cardiac electrodes in the esophagus, trachea, or within the heart itself. The first intracardiac electrode described, a saline-filled catheter, is used in conjunction with a unipolar monitoring system. As the catheter passes from superior vena cava through upper atrium, mid-atrium, and lower atrium, a series of changes in the ECG occur. In the vena cava the pattern resembles aVR with inverted P waves and QRS complex. As the catheter progresses through upper, mid, and lower atrium, the P wave progresses from inverted to biphasic to upright in the low atrium. This technique is limited primarily to correct positioning of catheters in the atria for air aspiration prior to high-risk surgical procedures. The lead system is limited by its suceptibility to AC current interference and low amplitude due to high resistances at the saline/blood interface.

A wire may also be passed percutaneously into the intra-atrial position. This yields an ECG tracing with a very large defined P wave and is much less prone to AC interference than the saline-filled catheter. The system is also resistant to electrocautery interference and functions well as a trigger for an intra-aortic balloon pump.

A further modification of the intracardiac wire, which allows more data to be collected, is the Multipurpose Pacing pulmonary artery catheter (Edwards Laboratories). This model of pulmonary artery catheter allows monitoring of pulmonary artery pressures, wedge pressure, thermodilution cardiac output, and in addition has three atrial electrodes and two ventricular electrodes that may be used for intracavitary ECG analysis, atrial and/or ventricular and even A-V sequential pacing, should it become necessary.[12]

There are hazards to invasive ECG monitoring not present in surface electrode systems. There is always a risk of complications during the electrode insertion, including carotid artery puncture, pneumothorax, vein laceration, atrial or ventricular perforation, sepsis, and so forth. More importantly, the patient is placed at risk for microshock. Therefore, before such techniques are used, one should ensure that the monitoring equipment has been tested and found to have a leakage current of less than 10 μA. Further, the insertion of a filter that blocks all frequencies greater than 20 kHz between the patient and monitor is advised.

As an alternative to intracardiac ECG leads, esophageal electrode systems (placed on the esophageal stethoscope) have been used.[9] These systems, which may be unipolar or bipolar, have the advantage of permitting a very good view of the posterior wall for ischemia detection as well as providing a large P wave for diagnosis of atrial dysrythmias that might otherwise be missed on standard surface electrodes. Its insertion and use is associated with a very low morbidity.

A subsequent modification of an esophageal lead exists as the intratracheal electrocardiogram lead. This lead is incorporated into an endotracheal tube and its electrogram patterns are similar to that of the esophageal electrode. It has been used primarily in the pediatric population.

DETECTION OF DYSRHYTHMIAS AND CONDUCTION DEFECTS

Since its inception as an intraoperative monitor, the ECG has been used in the detection and diagnosis of dysrythmias, which are very common occurrences during anesthesia in patients with and without cardiac disease. However, in patients with known cardiac disease, dysrythmias are more frequent and result in significant morbidity and mortality. Most dysrythmias occur during intubation and extubation, are not usually hemodynamically significant, and require no pharmacologic treatment.

Lead systems commonly employed for detection of rhythm disturbances include II, V_1, MCL_1, CB_5, and esophageal leads. These leads all produce clearly identifiable, upright P waves and well-defined QRS complexes. The esophageal lead may produce P waves so large as to make them difficult to differentiate from the QRS complex. Thus, a simultaneous surface ECG is used to identify the relationship of P waves to the QRS complexes (Fig. 3).

The cause of intraoperative dysrythmias are legion. Anesthetic agents, other drugs, central venous cannuation, surgical manipulation, vagal reflexes, and electrolyte abnormalities are among the more common etiologies. The reader is referred to more detailed reviews on this subject.

Central venous catheterization of the right atrium, right ventricle, or pulmonary artery is a cause of perioperative arrythmias. In this situation, premature atrial beats, atrial fibrillation, and ventricular ectopy can all be precipitated. These dysrythmias are usually, but not exclusively, transient and require no therapy.

Surgical maneuvers can also cause abnormalities of cardiac rhythm. Traction on the peritoneum during intra-abdominal procedures activates a strong vagal reflex resulting in bradydysrythmias. Similar reflexes are activated by pulling on the testicle and vas or pressure on the orbital contents. During neurosurgical procedures, manipulation in and around the brainstem may precipitate arrythmias of many types. Also, increases in intracerebral pressure can cause bradycardia through Cushing's reflex.

Recently, Krowka et al[11] have cited impressive evidence that myocardial ischemia itself can be a direct cause for cardiac dysrythmias in patients undergoing thoracotomy and that prompt, effective treatment of that ischemia caused the abnormal rhythm to cease.

Conduction abnormalities of the common left bundle branch are rarely benign and are often associated with significant coronary artery disease, cardiomyopathy, or aortic valvular disease. Depolarization of the right ventricle occurs normally with left ventricular depolarization occurring later. The ECG reflects this incoordination of depolarization with a broad (greater than 0.12 seconds) QRS, slurred rSR pattern in the lateral chest leads, and qrS pattern in right-sided leads.

Complete left bundle branch block has important clinical implications for the anesthesiologist. Conduction through the right bundle

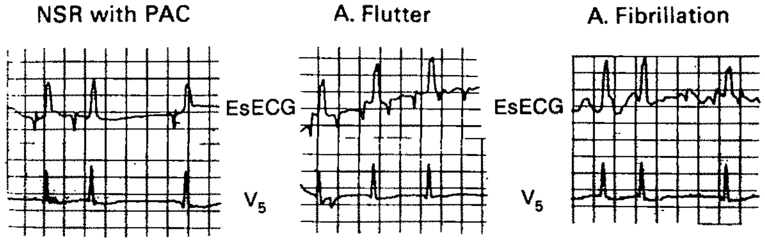


Figure 3. An esophageal lead (Es ECG) compared with lead V_5 during transition from sinus rhythm to atrial flutter and atrial fibrillation. Appropriate diagnosis is aided by having the Es ECG supplement the information obtained from lead V_5. The surface ECG (V_5) is used as a marker for identification of QRS complexes on the Es ECG. (*From* Griffin RM, Kaplan JA: ECG lead systems. *In* Thys DM, Kaplan JA (eds): The ECG in Anesthesia and Critical Care. New York, Churchill Livingstone, 1987; with permission.)

branch may be interupted transiently or permanently by a catheter traversing the right ventricle as in pulmonary artery catheterization.[14] This conduction abnormality may develop immediately on entry into the ventricle or after the catheter has been properly positioned in the pulmonary artery. In patients with pre-existing left bundle branch block, development of right heart block results in complete heart block and asystole or a slow ventricular escape rhythm. Therefore, it is our recommendation that in patients with left bundle branch block, provisions for immediate cardiac pacing either by invasive transvenous leads or noninvasive external cardiac pacing, be made available before pulmonary artery catheterization. Multipurpose Pacing pulmonary artery catheters or Paceport catheters (Edwards Laboratories) may not be sufficient safeguards, as the development of abnormal rhythm conduction defects and cardiovascular collapse may occur before the balloon floatation catheters are properly positioned: a prerequisite for their proper function.

DETECTION OF ISCHEMIA

The intraoperative detection of myocardial ischemia is a major indication for perioperative electrocardiography. Although not as sensitive or specific as some forms of more specialized monitoring equipment (for example, transesophageal echocardiography), more ischemic cardiac events are diagnosed by characteristic abnormalities of repolarization of the ECG than by any other method.

Electrically, ischemia first presents as repolarization abnormalities and ST depression. The T waves then become flattened or inverted. As ischemia progresses, the ST segment elevates, giving evidence of increasingly abnormal repolarization. The degree of ST-segment elevation correlates with the severity of the ischemia and the size of the area at risk. If reperfusion occurs, the electrical abnormalities tend to normalize. If, however, ischemia continues or worsens, Q waves develop in the leads near the infarcted area. The development of Q waves indicates the presence of irreversible, transmural necrosis without electrical activity.

As noted previously, most patients manifest early myocardial ischemia with ST-segment depression. Some patients, however, react atypically and present with initial ST-segment elevation without preceding depression.[6] The majority of these patients have suffered a myocardial infarction previously, and the ST elevations may represent segmental wall motion abnormalities or a ventricular aneurism. The exact etiology of the abnormal repolarization pattern is unclear.

About 30 per cent of the patients who present with initial ST-segment elevation have not had a previous infarction and are exhibiting the signs of variant (Prinzmetal's) angina (Fig. 4). Lastly, a small number of patients (0.2 to 1.7 per cent) have neither variant angina nor previous myocardial infarction. These patients with exercise-induced

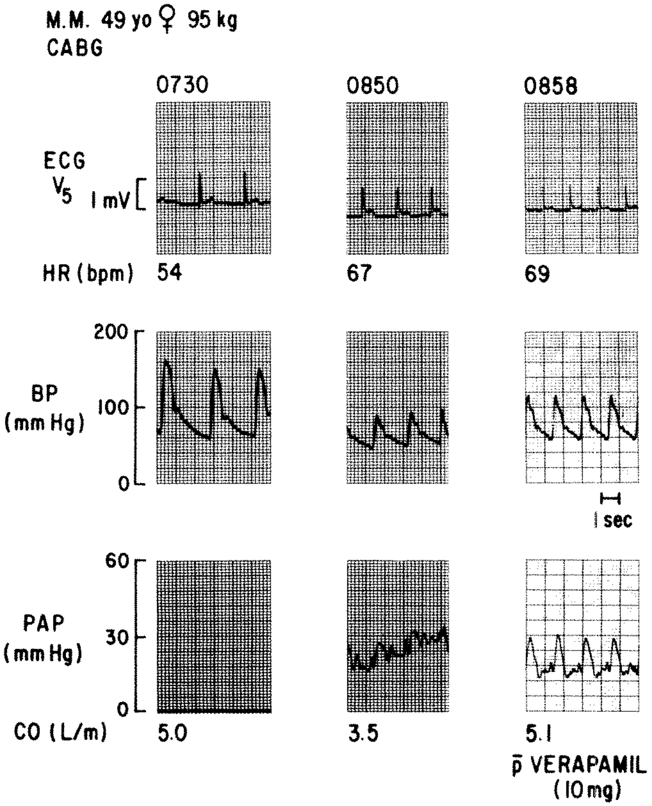


Figure 4. Intraoperative ECG, which demonstrates ST-segment elevation in lead V_5. The patient had a history of variant angina (vasospastic). ST elevations resolved with verapamil. (*From* Barash PG: Monitoring myocardial oxygen balance: Physiologic basis and clinical application. ASA Refresher Course, Washington, DC, May 21–23, 1983, pp 103/1–7; with permission.)

ST elevations have been found to have severe, high-grade stenosis of their coronary arteries. In these patients, ST-segment elevation in response to stress indicates a critical degree of coronary artery disease.

Blackburn and Katigbak[3] have shown during exercise electrocardiography that 89 per cent of ischemic events were detected by monitoring lead V_5. Sensitivity is further improved by concurrent monitoring of standard lead II and V_5. Using this dual lead monitoring system, 96 per cent of excerise-induced ischemia (by ECG) will be detected. Essentially 100 per cent of ischemic episodes can be detected by monitoring standard lead II, aVF, and V_{3-6}. Unfortunately, multiple lead placement and the large amount of data produced by this system make it impractical for use in the operating room.

A recent study by Wohlgelernter and colleagues[17] called this data (use of leads II/V_5) into question. Using echocardiography as the "gold standard" to detect ischemia, they compared 3-lead and 12-lead

ECG systems with echocardiography during percutaneous coronary angioplasty. At each stage of the angioplasty procedure the 12-lead ECG system detected approximately a 20 per cent greater incidence of ischemia than the 3-lead system. Such data suggests that the use of multiple leads increases the ECG's sensitivity to detection of ischemia. In the future, anesthesiologists may monitor more than one or two leads simultaneously, probably with computer assistance, to detect intraoperative ischemia.

Ischemia detection may be improved by considering the anatomic site of the lesions before choosing a specific lead system. A patient with significant disease in the left anterior descending coronary artery may develop anterior wall ischemia or infarction. Electrocardiographically, leads V_{2-3} would detect such ischemia best. Similarly, disease of the left circumflex artery would put the lateral wall of the left ventricle at risk. Ischemic changes would be detected in leads I, aVL, and V_{4-6}. If ischemia due to right coronary artery disease is suspected, the patient should be monitored for inferior wall ischemia (II, III, aVF) or even right ventricular ischemia or infarction (V_1 or V_{4R}).[13] Posterior ischemia or infarction may be very difficult to diagnose or detect. Subtle reciprocal changes may be present in the anterior leads or more specialized lead configurations such as intra-atrial or esophageal leads must be used.

There is no universally agreed upon ECG criteria for diagnosis of ischemia. ST-segment depression is considered significant if horizontal or downsloping and depressed 1 mm from the isoelectric line at a point 0.06 seconds from the J point (Fig. 5). Exercise and stress alone can cause ST-segment abnormalities. These repolarization abnormalities are usually confined to minor depression from the isoelectric line with an upsloping ST segment. However, an upsloping ST segment may be considered indicative of ischemia when the magnitude of the depression reaches 2 mm at a point 0.08 seconds from the J point.

Q waves also are nonspecific findings indicative only of electrical vectors of ventricular depolarization proceeding in a direction away from the ECG lead. Q waves are considered significant for infarction when they occur in more than one lead and exceed 0.03 seconds in duration.

NEWER ELECTROCARDIOGRAPHIC MODALITIES

The detection rate of dysrythmias and myocardial ischemia by electrocardiography has been recently improved by certain computer-assisted systems. Computer algorithms aid in recognition of dysrythmias on the basis of rate, interval duration, and length of time spent at the isoelectric line. Variation from certain preset values of any of these parameters results in an alarm condition, tentative dysrythmia identification, and the ECG complex is stored in memory for subsequent retrieval. Unfortunately, the operating room presents a difficult envi-

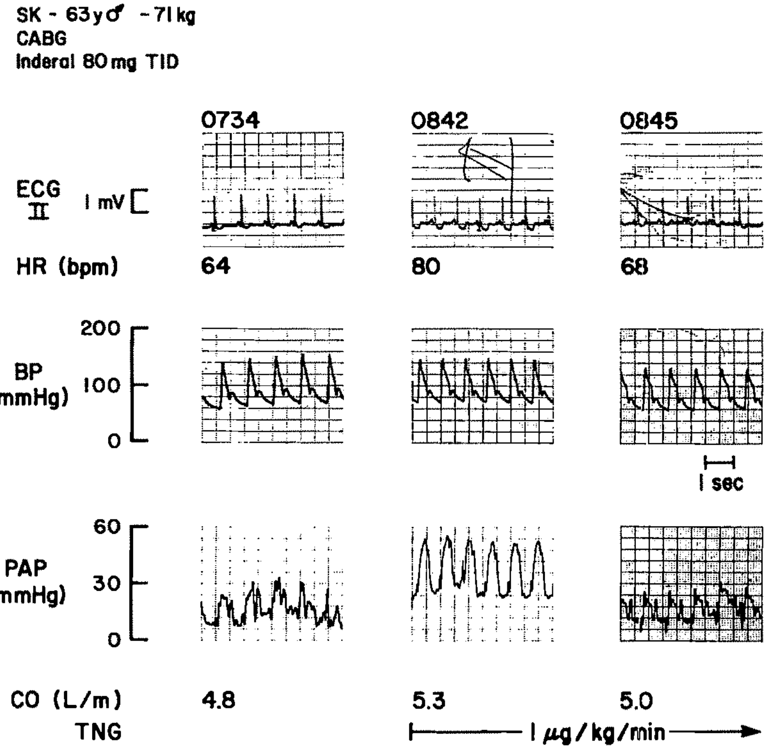


Figure 5. Intraoperative tracings obtained during an episode of myocardial ischemia. Note increasing pulmonary artery pressures and simultaneous downsloping ST segments in lead II. These changes reverted with intravenous nitroglycerine (TNG). CO = cardiac output. (*From* Barash PG: Monitoring myocardial oxygen balance: Physiologic basis and clinical application. ASA Refresher Course, Washington, DC, May 21–23, 1983, pp 103/1–7; with permission.)

ronment for this monitoring modality. Patient position, electrocautery, and other sources of electrical interference makes these computer-assisted dysrythmia-detection systems unreliable and prone to false-positive responses.

Computer-assisted analysis has also been employed for the detection of myocardial ischemia. Kotrly et al[10] modified an exercise electrocardiograph for ST-segment trending analysis that monitors multiple leads simultaneously. A microcomputer measures the deviation of the ST segment from the isoelectric line at the J point plus 60 ms and displays the absolute values for these deviations in multiple leads. These data may be displayed in real time as a digital display or alternatively displayed as trend line, which clearly shows changes in the ST segment over time (Fig. 6). Use of the ST-trend analyzer has been shown to improve the anesthesiologists' ability to detect myocardial ischemia intraoperatively as compared with more conventional ECG methods.[10] Also, the use of the trend line allows these data to be displayed in a simple yet effective manner. There are some

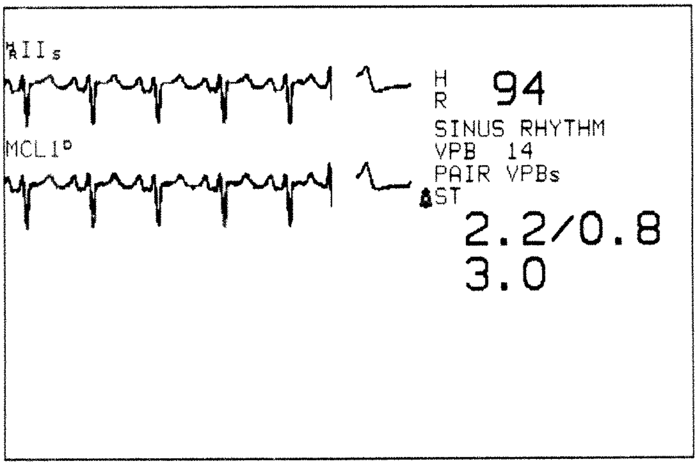


Figure 6. Data displayed from an ST-segment trend analyzer. Simultaneous ECG leads (II/MCL$_1$), heart rate, rhythm analysis, and variation of the ST segments from baseline are displayed. The computer analyses the ST segments and assigns a millimeter deviation from baseline for each lead and summates the total ST-segment deviation. II = 2.2 mm, MCL = 0.8 mm, total = 3.0 mm. (*From* Kotrly KJ, Kutter GS, Mortara D, et al: Intraoperative detection of myocardial ischemia with an ST segment trend monitoring system. Anesth Analg 63:343, 1984; with permission.)

difficulties with ST-trend analysis in the operating room. In order for the ST segments to be assessed, between 7 and 20 complexes are averaged for each determination. Unfortunately, a meaningful analysis then requires a number of normal complexes without artifact from any source. In the operating room environment, electrocautery and any number of other interfering influences may disable the ST-trend analyzer for variable periods of time. Abboud et al[1] have described a system of cross-correlation analysis in which a computer template of an ECG complex is stored. Subsequent complexes are compared with this template and otherwise inapparent changes in the surface ECG ST segments are recognized and displayed as variations of a trending line (Fig. 7).

SUMMARY

The ECG remains the prime monitor for the detection of dysrythmias or myocardial ischemia in the perioperative period. It is an inexpensive, easily applied, and easily interpreted monitoring system that can function throughout the operative period. No other single monitoring system can fulfill the ECG's function over such a wide range of clinical and surgical situations. Careful attention to detail in the calibration and lead selection and close attention to subtle repolarization changes make the ECG a versatile and adequate monitor of dysrythmias and ischemia. Computer-assisted methods will continue to improve the sensitivity of this time-proved monitoring modality.

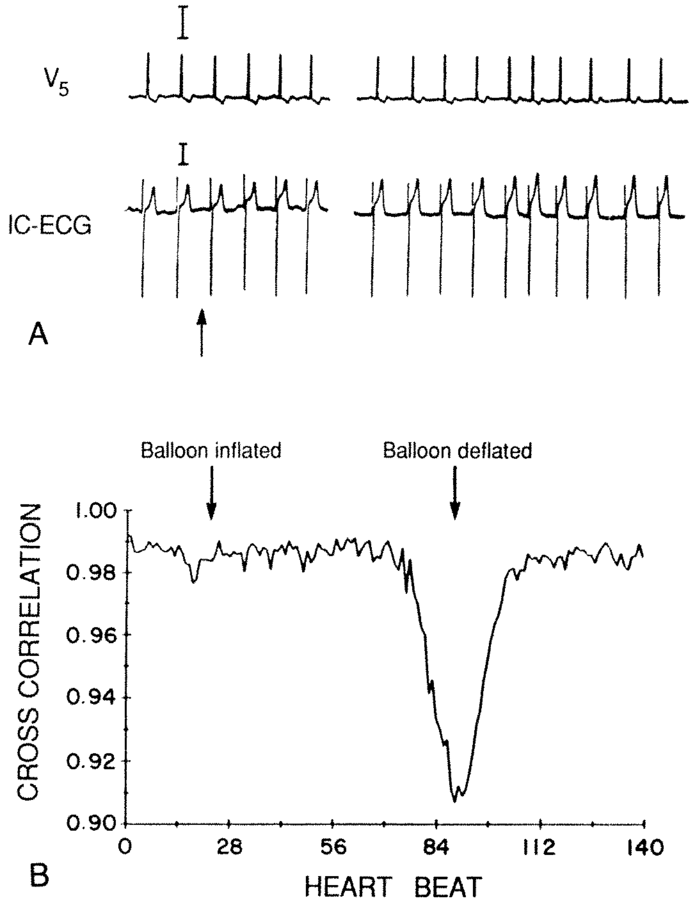


Figure 7. Simultaneous lead V_5 and coronary sinus ECG (IC – ECG) obtained at the start of a percutaneous coronary angioplasty procedure (*arrow*). During PTCA, V_5 shows no changes consistent with myocardial ischemia; however, IC-ECG shows significant ST-segment elevation. Cross-correlation analysis obtained from the surface ECG (V_5) shows a significant alteration of the ST segment (cross correlation 0.99 to 0.90). With release of PTCA balloon, ST segments return to normal. (*From* Abboud S, Cohen RJ, Selwjn A, et al: Detection of transient myocardial ischemia by computer analysis of standard and signal-averaged high-frequency electrocardiograms in patients undergoing percutaneous transluminal coronary angioplasty. Circulation 76:3, 1987; with permission.)

REFERENCES

1. Abboud S, Cohen RJ, Selwjn A, et al: Detection of transient myocardial ischemia by computer analysis of standard and signal-averaged high-frequency electrocardiograms in patients undergoing percutaneous transluminal coronary angioplasty. Circulation 76:3, 1987
2. Barash PG: Monitoring myocardial oxygen balance: Physiologic basis and clinical application. ASA Refresher Course, Washington, DC, May 21–23, 1983, pp 103/1–7
3. Blackburn H, Katigbak R: What ECG leads to take after exercise. Am Heart J 67:184, 1964

4. Cannard TH, Dripps RD, Helwig J, et al: The electrocardiogram during anesthesia and surgery. Anesthesiology 21:194, 1960
5. Chaitman BR, Hanson JS: Comparative sensitivity and specificity of excerise electrocardiographic lead systems. Am J Cardiol 47:1335, 1981
6. Chaitman BR, Waters DD, Theroux P, et al: ST segment elevation and coronary spasm in response to excerise. Am J Cardiol 47:1350, 1981
7. Goldberger E: Simple electrocardiographic electrode of zero potential and technique of obtaining augmented unipolar extremity leads. Am Heart J 23:483, 1942
8. Griffin RM, Kaplan JA: ECG lead systems. *In* Thys DM, Kaplan JA (eds): The ECG in Anesthesia and Critical Care. New York, Churchill Livingstone, 1987
9. Kates RA, Zaidan JR, Kaplan JA: Esophageal lead for intraoperative electrocardiographic monitoring. Anesth Analg 61:781, 1982
10. Kotrly KJ, Kutter GS, Mortara D, et al: Intraoperative detection of myocardial ischemia with an ST segment trend monitoring system. Anesth Analg 63:343, 1984
11. Krowka MJ, Pairolero PC, Trastek VF, et al: Cardiac dysrhythmia following pneumonectomy: Clinical correlates and prognostic significance. Chest 91:490, 1987
12. Lichtenthal PR: Multipurpose pulmonary artery catheter. Ann Thorac Surg 36:493, 1983
13. Roy WL, Edelist G, Gilbert B: Myocardial ischemia during non-cardiac surgical procedures in patients with coronary artery disease. Anesthesiology 51:393, 1979
14. Thomson IR, Dalton BC, Lappas DG: Right bundle branch block and complete heart block caused by the Swan-Ganz catheter. Anesthesiology 51:359, 1979
15. Thys DM: The normal ECG. *In* Thy DM, Kaplan JA (eds): The ECG in Anesthesia and Critical Care. New York, Churchill Livingstone, 1987
16. Wilson FN, Johnston FD, McLeod AG: Electrocardiograms that represent the potential variations of a single electrode. Am Heart J 9:447, 1934
17. Wohlgelernter D, Cleman M, Highman HA: Regional myocardial dysfunction during coronary angioplasty, evaluation by two dimensional echocardiography and 12-lead electrocardiography. J Am Coll Cardiol 7:1245, 1986
18. Zaidan JR: Electrocardiography. *In* Barash PG, Cullen B, Stoelting RK (eds): Clincial Anesthesiology. Philadelphia, Lippincott, 1989, pp 587–623

Department of Anesthesiology
Yale University School of Medicine
P.O. Box 3333
New Haven, CT 06510

Cumulative Index 1988

Volume 6

March	MANAGEMENT OF PATIENTS WITH MULTISYSTEM ORGAN FAILURE, pages 1–250
June	NEW ANESTHETIC DRUGS, pages 251–460
September	MYOCARDIAL ISCHEMIA AND PERIOPERATIVE INFARCTION, pages 461–654
December	CARDIAC MONITORING, pages 655–915

Note: Page numbers of issue and article titles are in **boldface** type.

Acute renal failure, **173–184**
  diagnosis of, 176–177
  etiology and prognosis of, 173–175
  nutrition in, 180
  pathophysiology of, 175–176
  treatment for, 178–181
Acute right ventricular failure, and pulmonary hypertension, 583–584
Adrenal and thyroid dysfunction, effect on central nervous system, 215–216
Adrenergic agents, effect of, on systemic responses to elective surgery, 226–227
Adult respiratory distress syndrome (ARDS), parenchymal dysfunction as cause of, 138–139
  patients with, importance of monitoring right ventricular function in, 857
Afferent neuronal stimuli, role of, in neuroendocrine response, 2–4
Age, effect on pharmacokinetics and pharmacodynamics, 253–255
Alfentanil, pharmacologic properties of, 319–322
Alkylphenols, pharmacokinetic profile and pharmacodynamic effects of, 310–315
Ambulatory ST-segment monitoring, as cardiac monitoring technique, 684–686
Amines, quaternary, pharmacologic properties of, 366
Amino acids, effect of, on ventilatory response, 64–66
4-Aminopyridine, an NMBA antagonist, 348
Amrinone, chemical structure of, 372
  intravenously administered, adverse effects and complications of, 378
    dosage of, 378–379
    electrophysiologic effects of, 377–378
    for management of congestive heart failure, 372–379
    hemodynamic effects of, 374–377
    interactions of, with anesthetics, 378
    mechanism of action of, 373–374
    metabolism and pharmacokinetics of, 373
Analgesia, epidural, in obstetrics, 444–446
  patient-controlled, in obstetrics, 443–444
Analgesics, narcotic, in obstetrics, 440–442
  opioid, **319–333**
Anaphylactoid reactions, to NMBAs, 343
Anemia, aplastic, critical care drugs associated with, in multisystem failure, 24
  hemolytic, critical care drugs associated with, 24
Anesthesia, effect on incidence of myocardial ischemia and infarction, 514–515
  effect on pharmacokinetics and pharmacodynamics, 252–253
  epidural, effect of, on systemic responses to elective surgery, 222–225
  inhalational, effect of, on systemic responses to elective surgery, 226

Anesthesia *(Continued)*
- inhalational, new developments in, **281–296**. See also *Anesthetics, inhaled*.
- intravenous, combinations of drugs used for, 305
  - drug combinations for, 315–316
  - induction agents for, hemodynamic effects during induction and postintubation, 301
    - incidence and side effects of, 300
    - induction characteristics of, 289
    - pharmacokinetic profiles of, 301
  - new developments in, **297–318**
  - pain during, effect of injection site on, 316
  - properties of an ideal drug, 297
- new drugs in, issue on, **251–456**
- psychotropic drugs in, new developments in, **419–438**. See also *Psychotropic drugs*.

Anesthetics, in prevention and treatment of myocardial ischemia, **593–613**
- general concepts, 593–595
- inhalation, in prevention and treatment of myocardial ischemia, 595–604
  - clinical studies, 603–604
  - in vitro studies, 602–603
  - in vivo studies, 595–602
- inhaled, and myocardial oxygen balance, 281–288
  - animal studies, 281–283
  - clinical studies, 283–288
  - and neuroanesthesia, 288–291
  - effect on intracranial pressures, 289–291
- intravenous, in prevention and treatment of myocardial ischemia, 604–608
  - human studies, 606–608
  - laboratory studies, 604–606
- local, currently available, advantages and disadvantages of, 357–358
  - new amino-amide-type agents, 358–360
  - new developments in, **357–370**
  - novel agents, 365–367
  - regional, 362–365
    - combination drugs and additives in, 364–365
  - topical, 361–362
- volatile, and the liver, 291–293

Angina, labetalol for treatment of, 396
- mixed, and ischemic heart disease, 473–474
- unstable, and ischemic heart disease, 472–473

Antacids, for prophylaxis of aspiration, 409–411

Anticholinergics, for prophylaxis of aspiration, 409

Antidiuretic hormone, effect of, on neuroendocrine response, 16

Aplasia, factors leading to, in multisystem failure, 23–24

Arachidonic acid metabolites, for resuscitation in hemorrhagic shock, 130–131

ARDS. See *Adult respiratory distress syndrome*.

Arrhythmias, esmolol for treatment of, 389

Arterial blood pressure measurement (noninvasive), in pediatric cardiac monitoring, 827–828

Arterial blood supply, anatomy of, 839–840

Arterial pressure monitoring, direct, in pediatric cardiac monitoring, 830–831

Arylcyclohexylamines, pharmacokinetic profile and pharmacodynamic effects of, 308–310

Aspiration, patients at risk for, 408–409
- prophylaxis of, drugs for, 409–414
- severity of, factors affecting, 407–408

Atracurium, pharmacologic properties of, 343–346

Atracurium infusion, 341

Atrial septal defects, Doppler echocardiography for detection of, 799

Auscultation, of Korotkoff sounds, as method of noninvasive blood pressure measurement, 722–723

Auscultatory systems, automated, as method of noninvasive blood pressure measurement, 723–724

Ayurvedic medicine, 658

Aztecs, preoccupation with life and death among, 656

Barbiturates, pharmacokinetic profile and pharmacodynamic effects of, 298–302

Bard alfentanil infuser, 275–276

Benzodiazepines, effects of, on coronary blood flow, 607–608
- in obstetrics, 442–443
- pharmacokinetic profile and pharmacodynamic effects of, 304–307

Bestatin, for analgesia in cancer patients, 330–331

Beta-adrenergic antagonists, 381
- chemical structure of, 382

Beta-blocking drugs, for treatment of myocardial ischemia and infarction, 575–578, 620
- pharmacologic properties of, 381

Biliary tract, dysfunction of, and multisystem organ failure, 193–194

Blood, for resuscitation in hemorrhagic shock, 128–129

Blood flow, physics of, 786–787

Blood oxygen carrying capacity, as cause of myocardial ischemia and infarction, 464–465

Blood pressure devices, 725
Blood pressure measurement, noninvasive, **721–741**
  nonocclusive methods, 731–739
    Cortronic device in, 738–739
    Finapres device in, 734–738
    Penaz method, 732–734
  occlusive methods, 722–731
    auscultation, 722–723
    automated auscultatory systems for, 723–724
    automated oscillometric devices for, 726–727
    infrasound for, 724–725
    oscillometry for, 725–726
    peripheral pulse detection for, 729–731
    pitfalls of, 731
Blood supply, arterial, anatomy of, 839–840
Blood velocity, Doppler measurement of, 786–793
Bowel, small, dysfunction of, and multisystem organ failure, 189–191
Brain, effect of hemorrhagic shock on, 123
Bupivacaine, epidural, in obstetrics, 445
  for cesarean section anesthesia, 447
Buprenorphine, as premedicant, 435
Butorphanol, as premedicant, 434–435

Calcium antagonists, for treatment of myocardial ischemia, 578–581
Calcium channel blockers, for treatment of myocardial ischemia and infarction, 623–624
Calcium metabolism, disorders of, effect on central nervous system, 214–215
Calibration, of monitoring devices, **707–716**
  analog displays in, 709
  data measurement in, 707–708
  data transduction in, 708–709
  digital displays in, 711–712
  ECG processing in, 712–713
  filtering in, 709–711
  pressure measurement in, 713–716
Cannulation, venous, central, complications of, 751–753
Carbohydrate utilization, regulation of, in sepsis, 99–100
Cardiac drugs, new developments in, **371–405**
  adrenergic antagonists, 379–398
  inotropic drug, 371–379
Cardiac failure, effect on central nervous system, 203–206
Cardiac imaging techniques, for monitoring coronary circulation, 847
Cardiac monitoring, device calibration in, **707–716**
  electrical safety in, **699–707**
  historical backdrop to, **655–681**
    Chinese: yin/yang, 657–658
    Egyptian: Isis/Orisis, 657
    Einthoven: string galvanometer, 660–662
    Greek: odd/even, 659
    Indians: Pitha/Kapha, 658
    Mesoamerican focus, 656
    Mesopotamian focus, 681–682
    modern: negative/positive, 659–660
  issue on, **655–889**
  of pediatric patient, **825–837**
    basic noninvasive monitoring, 826–830
      arterial blood pressure measurement in, 827–828
      cardiac output monitoring, 829–830
      ECG in, 826–827
      pulse oximetry, 828–829
      transcutaneous oxygen monitoring, 829
    invasive monitoring, 830–834
      cardiac output monitoring, 833
      direct arterial pressure monitoring, 830–831
      intracardiac pressure measurement, 831
      left atrial catheters, 832–833
      mixed venous oxygen saturation monitoring, 833
      pulmonary artery catheterization, 831–832
      two-dimensional echocardiography and color flow Doppler, 833–834
  preoperative, **683–698**
Cardiac output, **803–824**
  continuous thermal, determination of, 816–817
  definition of, 803
  Doppler measurements of, 793–795
  measurement of, Fick principle in, 804–807
    indicator-dilution technique for, 807–817
    laser Doppler velocimetry in, 819
    pulse contour for, 817–818
    systolic time intervals in, 818
    thoracic electrical impedance in, 819–820
    ultrasound in, 819
Cardiac output monitoring, invasive, in pediatric cardiac monitoring, 833
Cardiac output monitoring (noninvasive), in pediatric cardiac monitoring, 829–830
Cardiac surgery, evaluation of patients for, echocardiography for, 780–781
  for perioperative myocardial ischemia and infarction, **505–526**. See also *Myocardial ischemia, and myocardial infarction, perioperative.*

Cardiovascular dysfunction, in septic shock, **87–118**
Cardiovascular monitoring, physiologic basis of, **891–902**
Catecholamines, effects of, on metabolism, 9
 on neuroendocrine response, 6–10
 for resuscitation in hemorrhagic shock, 129
 for treatment of septic shock, 108
Catheters, coronary sinus flow, for monitoring coronary circulation, 843–847
 left atrial, in pediatric cardiac monitoring, 832–833
Central nervous system, effect of adrenal and thyroid dysfunction on, 215–216
 effect of cardiac failure on, 203–206
 effect of encephalopathy in pregnancy on, 210
 effect of endocrinologic disorders on, 211–215
 effect of hepatic failure on, 208–209
 effect of pancreatic encephalopathy on, 209–210
 effect of renal failure on, 206–208
Cesarean section, anesthesia for, 447–449
  general, 448–449
  intraspinal opioids for, 447–448
  regional, 447
Channel blockers, calcium, for treatment of myocardial ischemia and infarction, 623–624
 potassium, pharmacologic properties of, 366–367
Chinese: yin/yang, preoccupation with life and death among, 657–658
Chloroprocaine, epidural, in obstetrics, 445–446
Cimetidine, for prophylaxis of aspiration, 411–412
Circulation, collateral, role of, in myocardial ischemia and infarction, 464
 coronary, anatomy of, 839–840
  monitoring of, **839–850**
   methods of, 843–847
  physiology of, 840–843
   humoral influences, 842–843
   mechanical factors, 841–842
   metabolic control, 840–841
   neural factors, 842
 early Eastern theories of, 664
 early Western theories of, 664–666
 venous, monitoring of, **865–889**
Closed-loop infusion, 274–275
Coagulation defects, correction of, in hemorrhagic shock, 131
Coagulopathy, as cause of chronic liver disease, 28
 as cause of liver disease, 27–28
 as cause of malnutrition, in multisystem failure, 28–29
 caused by liver transplantation, 31–32
 consumptive, in multisystem failure, 29–30
Coarctation, labetalol for treatment of, 395
Colon, dysfunction of, and multisystem organ failure, 191
Color flow Doppler, in pediatric cardiac monitoring, 833–834
Color flow mapping, 792–793
Congenital heart disease, Doppler ultrasound for diagnosis and treatment of, 798–799
Coronary artery disease, inhaled anesthetics for, 283–288
 preoperative diagnosis of, and outcome, 528–530
Coronary artery stenosis, athersclerotic, and ischemic heart disease, 467–469
  morphologic characteristics of, 469–471
Coronary artery(ies), narrowing of, as cause of myocardial ischemia and infarction, 464
Coronary circulation. See *Circulation, coronary.*
Coronary collaterals, in experimental models, 491–493
Coronary sinus flow catheter, for monitoring coronary circulation, 843–847
Coronary spasm, effect on incidence of myocardial ischemia and infarction, 516–517
Coronary steal, experimental models of, **485–503**
 models of, versus anesthetics, 496–500
Coronary vasospasm, and ischemic heart disease, 471
 mechanisms of, 471
Cortronic device, for nonocclusive blood pressure measurement, 738–739

DADL, pharmacologic properties of, 330
Dezocine, for sedation, 435–436
 pharmacologic properties of, 329–330
Dialysis, for treatment of acute renal failure, 179
Diazepam, effect of, on coronary blood flow, 607–608
Diltiazem, for treatment of myocardial ischemia, 578–579
Dipyridamole thallium imaging, 687–692
 clinical studies of, 687–692
 theoretical basis of, 687
Disseminated intravascular coagulation (DIC), acute, in multisystem failure, 30–31
Dopamine, for treatment of acute renal failure, 179
 for treatment of septic shock, 108

Doppler, continuous wave, 788–789
  pulsed wave, 789–790
Doppler echocardiography, **785–802**
  for evaluation of valvular function, 795–799
  future directions in, 799–800
Doppler flow data, display of, 790–791
Doppler measurement of flows and pressure gradients, in pediatric cardiac monitoring, 833–834
Doppler measurements, of blood velocity, 786–793
    techniques of, 787–790
  of cardiac output, 793–795
  physical principles of, 785–786
Doppler principle, 785–786
Doxacurium, pharmacologic properties of, 345, 346–347
Drug infusions, intravenous, 268–276
Drug metabolism, effect of nutrient infusion on, 66–67
Drugs, anesthetic, in prevention and treatment of myocardial ischemia, **593–613**
  in anesthesia, issue on, **251–456**
  vasoactive, in prevention and treatment of myocardial ischemia, **569–591**

ECG. See *Electrocardiogram, Electrocardiography.*
Echocardiography, Doppler, **785–802**. See also *Doppler measurements.*
  for detection of intracardiac air, 779–780
  for evaluation of patients for heart surgery, 780–781
  in diagnosis of myocardial ischemia, 509
  M-mode, in evaluation of global ventricular function, 772–775
  perioperative, **769–783**
  two-dimensional, in detection of myocardial ischemia and infarction, 556–559, 562
    in evaluation of global ventricular function, 775–776
    in evaluation of regional ventricular function, 776–779
Edrophonium, an NMBA antagonist, 348
EE measurement, interpretation of, in critically ill patients, 44–45
Efferent humoral response, role of, in neuroendocrine response, 4–18
Egyptians: Isis/Orisis, preoccupation with life and death among, 657
Einthoven: string galvanometer, preoccupation with life and death among, 660–662
Electrical safety, and device calibration, **699–719**
  in hospitals, 703–706
  in households and industry, 701–703
  principles of, 707
Electricity, basis of, 699–700
Electrocardiogram, in pediatric cardiac monitoring, 826–827
Electrocardiographic monitoring techniques, 683–686
  clinical studies of, 685–686
  theoretical basis of, 683–685
Electrocardiography, in detection of myocardial ischemia and infarction, sensitivity of, 562, **903–915**
  in diagnosis of myocardial ischemia, 507–508, 909–911
  in preoperative diagnosis of coronary artery disease, 528–530
  lead systems for ischemia detection, 545–546, 903–907
Electrocautery, and burn at patient attachment, 706–707
Electrocution, pathophysiology of, in cardiac monitoring, 700–701
Encephalopathy, complicating pregnancy, effect on central nervous system, 210
  pancreatic, effect on central nervous system, 209–210
Endocrinologic disorders, effect on central nervous system, 211–215
Energy expenditure estimation, from standard formulas, in critically ill patients, 43–44
Energy expenditure measurements, in critically ill patients, 41–43
Energy metabolism, in stress, 52–53
Enflurane, and hepatic injury, 291–292
  beneficial effects of, during myocardial ischemia, 595
  effect of, on incidence of myocardial ischemia and infarction, 515
  for consistent preservation of myocardial lactate extraction and hemodynamic stability, 284
Equilibrium gated pool scan, for monitoring right ventricular function, 854
Esmolol, 381–390
  adverse effects and complications of, 389
  dose and route of administration of, 390
  electrophysiologic effects of, 386–387
  for treatment of myocardial ischemia and infarction, 621–622
  hemodynamic effects of, 384–386
  interactions of, with anesthetics, 387–388
  mechanism of action of, 383–384
  metabolism and pharmacokinetics of, 382–383
  physiochemical characteristics of, 382
  respiratory effects of, 387
  uses of, 388–389

Etomidate (Amidate), in prevention and treatment of myocardial ischemia, 608
  pharmacokinetic profile and pharmacodynamic effects of, 302–304
Exercise stress testing, as cardiac monitoring technique, 683–686

Famotidine, for prophylaxis of aspiration, 412
Fasted state, effects of nutrients on reversal of, 51–52
Fat metabolism, during oxygen deficiency, 104–105
  during stressed starvation, 53–54
Fentanyl, effects of, on coronary blood flow, 606–607
  epidural, in obstetrics, 444–445
  in obstetrics, 441
Fiber optic dye detection, for measurement of cardiac output, 816
Fick principle, in measurement of cardiac output, 804–807
Finapres device, for nonocclusive blood pressure measurement, 734–738
First pass technique, for monitoring right ventricular function, 854
Furosemide, for treatment of acute renal failure, 178–179

Galvanometer, string, preoccupation with life and death among, 660–662
Gastrointestinal tract, drugs affecting, new developments in, **407–417**
  effect of hemorrhagic shock on, 123
Glucagon, effect of, on neuroendocrine response, 13–14
Glucocorticoids, effect of, on metabolism, 7–8
Glucose metabolism, during stress, 53
Glucose transport, characteristics of, 98
Glucose utilization, effect of increased cardiac work on, 100–101
Graded responses, 260–261
Gravity-flow manual IV system, 867–870
Greek: odd/even, preoccupation with life and death among, 659
Growth hormone, effects of, on metabolism, 11
    on neuroendocrine response, 10–11

Halothane, beneficial effects of, during myocardial ischemia, 595–602
  effect on incidence of myocardial ischemia and infarction, 515
  for coronary autoregulation, 284
Heart, as center for cardiac monitoring, Mesoamerican focus, 656
  effect of hemorrhagic shock on, 121–122
  in sepsis, 89–105
Heart rate, increases in, prevention and treatment of, in noncardiac surgical patients, 538–540
  role of, in myocardial ischemia and infarction, 465
Hematologic abnormalities, caused by septic shock, 80
Hematopoietic system, disorders of, in multisystem failure, 23–32
Hemodynamic pressure monitoring, 745–751
Hemofiltration, for treatment of acute renal failure, 179
Hemolysis, drug-induced, factors leading to, in multisystem failure, 24
Hemolytic uremic syndrome, and coagulation disorders, 31–32
Hemorrhagic shock, effect of, on neutrophil function, 33
Hemorrhage, response of body systems to, 120
Hemorrhagic shock, **119–134**
  and multisystem failure, treatment of, 125–131
  clinical assessment of, 123–124
  coagulation defects in, correction of, 131
  effect of, on brain, 123
    on gastrointestinal tract, 123
    on heart, 121–122
    on kidneys, 123
    on liver, 122–123
    on lungs, 122
  invasive assessment of, 124–125
  pathophysiology of, 119–121
  resuscitation in, 126–131
    arachidonic acid metabolites for, 130–131
    blood for, 128–129
    catecholamines for, 129
    fluids for, 126–129
    steroids for, 129–130
  treatment of, total parenteral nutrition for, 125–126
Hemostasis, abnormalities of, in multisystem failure, 27–32
  normal, 27
Hepatic failure, effect on central nervous system, 208–209
Hepatoscopy, in Assyro-Babylonian medicine, 656
Histamine H2 receptor antagonists, for prophylaxis of aspiration, 411–414
Hydromorphone, in obstetrics, 441
Hyperglycemia, effect on central nervous system, 211–212
Hypernatremia, effect on central nervous system, 212–213

Hypertension, esmolol for treatment of, 388
  perioperative, labetalol for treatment of, 395
  pregnancy-induced, labetalol for treatment of, 395–396
  pulmonary, acute right ventricular failure and, 583–584
Hypertensive emergencies, labetalol for, 394
Hyponatremia, effect on central nervous system, 213–214
Hypotension, controlled, isoflurane and, 289
Hypothalamic-pituitary-adrenal axis, effect of, on neuroendocrine response, 5–6
Hypoxia, effect on myocardial metabolism, 101–103

Imidazoles, pharmacokinetic profile and pharmacodynamic effects of, 302–304
Immune system, alterations in, in multisystem failure, 32–35
Indians: Pitha/Kapha, preoccupation with life and death among, 658
Indicator-dilution technique, in measurement of cardiac output, 807–817
  accuracy and precision, 809–814
  limitations, 814–815
  principles, 807–809
  recent developments, 816–817
Indomethacin, as tocolytic agent, 451
Inert gas washout technique, for monitoring coronary circulation, 843
Infrasound, as method of noninvasive blood pressure measurement, 724–725
Inotropes, for treatment of myocardial ischemia, 585
Insulin, effect of, on metabolism, 13
  on neuroendocrine response, 11–13
Intra-aortic balloon pump, for treatment of myocardial ischemia and infarction, 625–626
Intracardiac air, echocardiography for detection of, 779–780
Intracardiac pressure measurement, in pediatric cardiac monitoring, general considerations, 831
Intracranial pressure, increases in, following administration of inhaled anesthetics, 289–291
Intramyocardial pressure, role of, in myocardial ischemia and infarction, 463
Intravenous fat emulsions (IVFE), effects of, on lungs, in acutely ill patients, 63–64
Intravenous fluid administration, monitoring of, **865–889**
  with commercially available controllers and pumps, 884–885
Ischemia, effect on myocardial metabolism, 101–103
  in surgery for congenital lesions, incidence of, 513
  myocardial. See *Myocardial ischemia*.
    esmolol for treatment of, 389
  right ventricular, incidence of, 512–513
  silent, characteristics and significance of, 553–556
    incidence of, 511–512
Isoflurane, and cerebral protection, 288–289
  and controlled hypotension, 289
  and opioids, in patients with coronary artery disease, 286–287
  as arteriolar vasodilator in dogs, 282–283
  effect of, on incidence of myocardial ischemia and infarction, 514–515
  effect on myocardial oxygen balance, 285–286
  effects of, on coronary blood flow, 599–601
Isotopes, for monitoring coronary circulation, 847

Ketamine, pharmacokinetic profile and pharmacodynamic effects of, 308–310
Kidneys, dysfunction of, caused by spetic shock, 80
  effect of hemorrhagic shock on, 123

Labetalol, 390–398
  adverse effects and complications of, 396–397
  chemical structure of, 392
  dosage of, 397
  electrophysiologic effects of, 394
  hemodynamic effects of, 392–394
  interactions of, with anesthetics, 394
  mechanism of action of, 391–392
  metabolism and pharmacokinetics of, 391
  physiochemical characteristics of, 390
  uses of, 394–396
Laser Doppler velocimetry, in measurement of cardiac output, 819
Laudanosine, production of, effect on anesthetic requirement, 341–342
12-Lead ECG, as cardiac monitoring technique, 683–686
Left ventricular ejection fraction, assessment of, 692–695
  clinical studies of, 692–695
  theoretical basis of, 692
Lesions, atherosclerotic, morphologic characteristics of, 469–471
  of small bowel, and multisystem organ failure, 189–191
  regurgitant, Doppler measurement of, 797–798

Levophed, for treatment of septic shock, 108
Lidocaine, as topical anesthetic, 361–362
Liver, as center for cardiac monitoring,
    Mesopotamian focus, 655–656
  dysfunction of, and multisystem organ failure, 194–197
    caused by septic shock, 80
  effect of hemorrhagic shock on, 122–123
  effect of volatile anesthetics on, 291–293
Liver disease, and coagulopathy, 27–28
  chronic, and coagulopathy, 28
Liver transplantation, and coagulopathy, 31–32
Lorazepam, in obstetrics, 442
Lung injury, acute, hemodynamic abnormalities in, 142–144
    management of, 150
Lungs, edema of, effect of hemodynamics on, 140–142
  effect of hemorrhagic shock on, 122
Lymphocyte function, effect of trauma on, 33–34

Malnutrition, and coagulopathy, 28–29
Mannitol, for treatment of acute renal failure, 178
Meptazinol, pharmacologic properties of, 327–329
Mesopotamians, preoccupation with life and death among, 655–656
Metabolic brain disease, causes of, 205–206
Metabolic indicators, in diagnosis of myocardial ischemia, 509
Metabolic response, monitoring of, in multisystem organ failure, **39–47**
  to starvation, in acutely ill patients, 50
  to stress, in acutely ill patients, 52
Metabolism, drug, effect of nutrient infusion on, 66–67
  effect of glucocorticoids on, 7–8
  effects of catecholamines on, 9
  effects of glucocorticoids on, 6
  effects of growth hormone on, 11
  effects of insulin on, 13
  effects of neuroendocrine stress response on, **1–22**
  energy, in stress, 52–53
  glucose, during stress, 53
Methoxyflurane, for long-duration local analgesia, 365
Metkephamid, pharmacologic properties of, 330
Metoclopramide, for prophylaxis of aspiration, 413–414
Midazolam, 421–429
  as premedicant, 427–428
  effects of, on coronary blood flow, 607–608
  for conscious sedation, 428–429
  in obstetrics, 442–443
  mechanism of action of, 422–425
  pharmacokinetics of, 425–426
Mivacurium, pharmacologic properties of, 343–344
Mivacurium infusion, 342
Mixed venous oxygen saturation monitoring, in pediatric cardiac monitoring, 833
Morphine, in obstetrics, 440
Multisystem organ failure, anesthetic techniques for modification of systemic responses in, **221–235**
  cardiovascular dysfunction in, **87–118**. See also *Septic shock, cardiovascular dysfunction in.*
  hematologic and immunologic abnormalities associated with, **23–37**
  hemorrhagic shock in, treatment of, 125–131
  hepatic and splanchnic response in, **185–202**
  management of patients with, **1–235**
  metabolic response in, monitoring of, **39–47**
  neurologic complications of, **203–219**. See also *Central nervous system.*
  pulmonary dysfunction in, **135–172**. See also *Pulmonary dysfunction, in multisystem organ failure.*
Muscle and plasma AA profiles, in acutely ill patients, 54–59
Myasthenia gravis, patients with, atracurium and vecuronium in, 346
Myocardial blood flow, regional, role of, in myocardial ischemia and infarction, 465–467
Myocardial contraction, terms used to describe, 559
  phases of, 893–894
Myocardial infarction, acute, cardiologic reperfusion treatment for, **631–649**
    labetalol for treatment of, 396
    pathophysiology of, 632–634
  and myocardial ischemia, mechanisms of, **461–484**. See also *Myocardial ischemia, and myocardial infarction.*
  postoperative, diagnosis of, 536–537
  reperfusion during, factors affecting outcome-advisability of, 493–496
Myocardial ischemia, and myocardial infarction, detection of, **545–567**
      automated ST-segment analysis in, 549–553
      by measurement of pulmonary artery pressure, 563–564
      by two-dimensional echocardiography, 556–559, 562
      electrocardiographic lead systems for, 545–546

electrocardiography for, sensitivity of, 562
ST-segment depressions in, 546–549
in subendocardium, 465–467
mechanisms of, **461–484**
metabolic intervention in, 624–625
myocardial oxygen supply and demand in, 461–465
perioperative, and cardiac surgery, **505–526**
and noncardiac surgery, **527–543**
diagnosis of, 506–511
echocardiography in, 509
electrocardiography in, 507–508
intraoperative, 506–510
metabolic indicators in, 509
postoperative, 510–511
scintigraphy in, 508
ventricular filling pressure in, 508–509
etiology of, 513–514
factors associated with, 506
in noncardiac surgical patients, risk factors and outcome in, 532–536
incidence of, 511–517
anesthesia affecting, 514–515
coronary spasms and, 516–517
hemodynamic changes affecting, 515–516
inadequate myocardial preservation and, 517
management of, 518–520
outcome following, 520–521
prevention of, 517–518
prevention and treatment of, vasoactive drugs in, beta blockers, 575–578
nitroprusside, 573–574
regional myocardial blood flow in, 465–467
role of platelets and prostaglandins in, 474–478
treatment of, **615–630**
and perioperative infection, issue on, **461–649**
atherosclerotic coronary artery stenosis and, 467–469
coronary vasospasm and, 471
critical stenosis and, 469
esmolol for treatment of, 389
experimental models of, **485–503**
intraoperative, significance of, 564–565
treatment of, 537–538
intraoperative monitors of, 509–510
monitoring of, practical aspects of, 565
prevention and treatment of, role of anesthetic drugs in, **593–613**
vasoactive drugs in, **569–591**
calcium antagonists, 578–581
inotropes, 585
nitroglycerin, 569–573
vasoconstrictors, 581–583
reperfusion injury and, 478–480
silent, 474, 530–531
Myocardial metabolism, effects of ischemia and hypoxia on, 101–103
Myocardial muscle mechanics, 892–893
Myocardial oxygen balance, inhaled anesthetics and, 281–288
Myocardial oxygen demand, major determinants of, 462
Myocardial oxygen supply, autoregulation of, 462–463
blood oxygen carrying capacity in, 464–465
collateral circulation in, 464
coronary artery narrowing in, 464
heart rate in, 463
intramyocardial pressure in, 463
role of, in myocardial ischemia and infarction, 461–465
Myocardial perfusion imaging, 686–687
Myocardial salvage, in experimental models, 486–490
Myocardium, energy generation in, during sepsis, 96–98
fuel utilization in, during sepsis, 98–99

Nalbuphine, as premedicant, 435
in obstetrics, 441
Nalmefene, pharmacologic properties of, 325
Nalorphine, pharmacologic properties of, 326
Naloxone, pharmacologic properties of, 324–325
Naltrexone, pharmacologic properties of, 325
Narcotics, effect of, on systemic responses to elective surgery, 225–226
Neuroanesthesia, inhaled anesthetics and, 288–291
Neuroendocrine stress response, metabolic effects of, **1–22**
role of afferent neuronal stimuli in, 2–4
role of efferent humoral response in, 4–18
Neuromuscular blocking agents (NMBAs), anaphylactoid reactions in, 343
antagonists of, 347–348
cardiovascular side effects of, 342–343
cumulation in, 339
dose response of, 338–339
duration of action of, 335–337
infusions in, 339–342
long-acting, 346–347
of intermediate duration, 344–346
of short duration, 343–344
of ultrashort duration, 343
onset of action of, 338

Neutropenia, acquired, critical care drugs associated with, in multisystem failure, 25
    factors leading to, in multisystem failure, 24–25
Neutrophil function, effect of hemorrhagic shock on, 33
Nifedipine, for treatment of myocardial ischemia, 578–579
Nitroglycerin, for treatment of myocardial ischemia, 569–573, 616–620
Nitroprusside, for treatment of myocardial ischemia, 573–574
Nitrous oxide, and narcotics, effect on coronary artery disease patients, 287
NMBAs. See *Neuromuscular blocking agents.*
Nuclear magnetic imaging, for monitoring right ventricular function, 857
Nutrients, effect of, on reversal of fasted state, 51–52
  infusion of, effect on drug metabolism, 66–67
Nutrition, in acute renal failure, 180
  in acutely ill patients, **49–71**
  role of, in cell-mediated immunity, 32–33
  total parenteral. See *Total parenteral nutrition.*
Nutritional support, future aspects of, in acutely ill patients, 63–66
  in postoperative period, 59–62

Obstetrics, drugs used in, new developments in, **439–456**
    for cesarean section, 447–449
    systemic medication, 440–443
    benzodiazepines, 442–443
    mode of administration of, 440
    narcotic analgesics, 440–442
    uterine active agents, 449–451
  epidural analgesia in, 444–446
  patient-controlled analgesia in, 443–444
Open-loop infusion, 269–273
Opiates, endogenous, effect of, on neuroendocrine response, 14–15
Opioid agonist-antagonists, pharmacologic properties of, 325–327
Opioid agonists, pharmacologic properties of, 319–324
Opioid antagonists, pharmacologic properties of, 324–325
Opioid peptides, pharmacologic properties of, 330–331
Opioid(s), intraspinal, for cesarean section anesthesia, 447–448
  isoflurane and, in patients with coronary artery disease, 286–287
ORG 7617, 343
ORG 9273, 344
ORG 9426, 344
ORG 9616, 343
Organ failure, multisystem, management of patients with, **1–235**. See also *Multisystem organ failure.*
Oscillometric devices, automated, as method of noninvasive blood pressure measurement, 726–727
Oscillometry, as method of noninvasive blood pressure measurement, 725–726
  accuracy of, 727–729
Oxazepam, in obstetrics, 442
Oxygen deficiency, fat metabolism during, 104–105
Oxygen metabolism, disorders of, in septic shock, 88–89
Oxygen monitoring, transcutaneous, in pediatric cardiac monitoring, 829
Oxygen transport and utilization, abnormalities of, in multisystem failure, 144–147
Oxygen-derived free radical scavenge, for treatment of myocardial ischemia and infarction, 625
Oxymorphone, in obstetrics, 441
Oxytocin, as uterine active agent, 449

Pancreas, dysfunction of, and multisystem organ failure, 192–193
Paralysis, muscle, for treatment of pulmonary dysfunction in multisystem organ failure, 162–163
Parenchymal dysfunction, and ARDS, 138–139
Pediatric patients, cardiac monitoring for, **825–837**. See also *Cardiac monitoring, of pediatric patient.*
Penaz method, for nonocclusive blood pressure measurement, 732–734
Percutaneous transluminal coronary angioplasty (PTCA), for treatment of acute myocardial infarction, 637–639
Perfusion, historical backdrop to, 662–669
  Chinese vessels, 663
  eastern theories of circulation, 664
  Egyptian pneumatics, 663
  Greek distinctions, 663–664
  stethoscopy in, 666–669
  western theories of circulation, 664–666
Perioperative echocardiography, examination by, 771–772
Pharmacodynamics, and pharmacokinetics, new developments in, **251–280**. See also *Pharmacokinetics, and pharmacodynamics.*
Pharmacogenetics, effect on pharmacokinetics and pharmacodynamics, 255–256

Pharmacokinetic-pharmacodynamics models, 259–267
Pharmacokinetics, and pharmacodynamics, factors influencing, 252–258
  new developments in, **251–280**
  population, approaches to estimating, 258–259
Pheochromocytoma, labetalol for treatment of, 395
Pipecuronium, pharmacologic properties of, 345, 346–347
Pituitary-gonadal axis, effect of, on neuroendocrine response, 17–18
Pituitary-thyroid axis, effect of, on neuroendocrine response, 16–17
Platelet dysfunction, factors leading to, in multisystem failure, 26–27
Platelet(s), role of, in myocardial ischemia and infarction, 474–478
Positive end-expiratory pressure (PEEP), in ARDS, 158–166
Potassium channel blockers, pharmacologic properties of, 366–367
Pregnancy, encephalopathy complicating, effect on central nervous system, 210
Pregnancy-induced hypertension, labetalol for treatment of, 395–396
Premedicants, new narcotic drugs as, 434–436
Premedication, ideal, 420–421
Pressure-flow relationship, 870–877
  extravasation and, 877–881
  obstructions and, 881–883
Pressure-flow-resistance relationship, 866–870
Propofol (Diprivan), pharmacokinetic profile and pharmacodynamic effects of, 310–315
Propranolol, for treatment of myocardial ischemia and infarction, 575–576
Prostaglandin E_1, for treatment of pulmonary dysfunction in multisystem organ failure, 163
Prostaglandins, E and F series, as abortifacients in obstetrics, 449–450
  effects of, on lungs, in acutely ill patients, 63–64
  role of, in myocardial ischemia and infarction, 474–478
Psychotropic drugs, categories of, 419–420
  new developments in, **419–438**
PTCA. See *Percutaneous transluminal coronary angioplasty.*
Pulmonary artery, catheter presence in, complications of, 754–755
Pulmonary artery catheter, passage of, complications of, 753–754
Pulmonary artery catheter monitoring, **743–767**
  clinical application of, 761–763
  data measurement and interpretation in, 744–745
  hemodynamic pressure monitoring in, 745–751
  physical complications of, 751–755
Pulmonary artery catheterization, in pediatric cardiac monitoring, 831–832
Pulmonary artery pressure(s), in detection of myocardial ischemia and infarction, 563–564
Pulmonary capillary wedge pressures, measurement of, in diagnosis of subendocardial ischemia, 563–564
Pulmonary dysfunction, in multisystem organ failure, **135–172**
  abnormalities of oxygen transport and utilization in, 144–147
  bedside hemodynamic measurements, 151–153
  clinical and pathologic correlations, 147–150
  effect of hemodynamics on lung edema and gas exchange in, 140–142
  hemodynamic management of, 153–154
  invasive hemodynamic monitoring in, 150–151
  muscle paralysis for treatment of, 162–163
  prostaglandin E_1 for treatment of, 163
  steroids for treatment of, 161
  ventilatory management of, 155–161
Pulsation, direct measurement of, historical backdrop to, 672
  historical backdrop to, 669–677
    Chinese, 670
    Egyptian, 669–670
    Greek, 671–672
    Indian, 670–671
  indirect measurement of, historical backdrop to, 675–677
  venous access and, historical backdrop to, 672
Pulse contour, in measurement of cardiac output, 817–818
Pulse detection, peripheral, as method of noninvasive blood pressure measurement, 729–731
Pulse oximetry, in pediatric cardiac monitoring, 828–829

Quantal responses, 260

Ranitidine, for prophylaxis of aspiration, 412
Renal failure, effect on central nervous system, 206–208
Renin-angiotensin system, effect of, on neuroendocrine response, 15–16

Reperfusion, and regional wall motion, 561–562
  during myocardial infarction, factors affecting outcome–advisability of, 493–496
  experimental models of, **485–503**
Reperfusion injury, and ischemic heart disease, 478–480
Reperfusion treatment, cardiologic, for acute myocardial infarction, **631–649**
  for acute myocardial infarction, and improvement of prognosis, 642–646
    beneficial effects of, 639–642
    PTCA for, 637–639
    thrombolytic therapy, 635–637
Respiratory muscle failure, in shock, 135–138
Resuscitation, in hemorrhagic shock, 126–131
Reticuloendothelial system, effect of trauma on, 33
Right ventricular function, monitoring of, **851–863**
    complications of, 858–859
    importance of, in management of patients with ARDS, 857
    nuclear magnetic imaging for, 857
    radionuclear techniques for, 854
    thermodilution technique for, 855–856
    two-dimensional echocardiography for, 855
Ropivacaine, pharmacologic properties of, 358–360
RQ measurement, interpretation of, in critically ill patients, 44–45

Saxitoxin (STX), pharmacologic properties of, 366
Scintigraphy, in diagnosis of myocardial ischemia, 508
Sepsis, early versus late, in acutely ill patients, 61
  heart in, mechanics of, 89–95
    myocardial perfusion and metabolism of, 95–105
  pulmonary abnormalities associated with, 139
Septic shock, **73–85**
  cardiovascular dysfunction in, **87–118**
    effect on pulmonary circulation, right ventricle, and respiratory pump, 105–107
    management of, 107–108
    oxygen metabolism in, 88–89
  cardiovascular effect of, 75–80
  clinical manifestation of, 74
  diagnosis of and therapy for, 81–82
  organ dysfunction caused by, 80–81
  pathophysiology of, 74–75
  pulmonary damage caused by, 80
Sevoflurane, effects of, 292–293
Shock, hemorrhagic, **119–134**. See also *Hemorrhagic shock.*
  respiratory muscle failure in, 135–138
  septic, **73–85**. See also *Septic shock.*
"Simplitrol" Portable Model Cambridge Electrocardiograph, 662
Skeletal muscle relaxants, new developments in, **335–355**. See also *Neuromuscular blocking agents (NMBAs).*
Starvation, in the nonstressed state, 50
  metabolic response to, in acutely ill patients, 50
  stressed, fat metabolism during, 53–54
  stressed vs. unstressed, 61
Stenosis, aortic, Doppler evaluation of, 796–797
  atherosclerotic coronary artery, and ischemic heart disease, 467–469. See also *Coronary artery stenosis, atherosclerotic.*
  critical, and ischemic heart disease, 469
  mitral, Doppler evaluation of, 797
  valvular, Doppler evaluation of, 795–796
Stereoisomers, effect on pharmacokinetics and pharmacodynamics, 256–258
Steroids, for resuscitation in hemorrhagic shock, 129–130
  for treatment of pulmonary dysfunction in multisystem organ failure, 161
Stethoscopy, early history of, 666–669
Stewart-Hamilton equation, 756
Stomach, dysfunction of, and multisystem organ failure, 186–189
Stress, glucose metabolism during, 53
  late, and multisystem organ failure, 62
  metabolic response to, in acutely ill patients, 52
ST-segment analysis, automated, in detection of myocardial ischemia and infarction, 549–553
ST-segment depression, in detection of myocardial ischemia and infarction, 546–549
ST-segment monitoring, in preoperative diagnosis of myocardial ischemia in noncardiac surgical patients, 529–530, 531
Subendocardium, and ischemia, 465–467
Sufentanil, effects of, on coronary blood flow, 607
  in obstetrics, 441
  pharmacologic properties of, 323–324
Surgery, cardiac, for perioperative myocardial ischemia and infarction, **505–526**. See also *Myocardial ischemia, and myocardial infarction, perioperative.*
  elective, systemic responses to, anesthetic modification of, 222–228

  noncardiac, for perioperative myocardial ischemia and infarction, **527–543**. See also *Myocardial ischemia, and myocardial infarction, perioperative.*
Surgical injury, systemic responses to, 221–228
Systolic time intervals, in measurement of cardiac output, 818

Tachycardia, perioperative, esmolol for treatment of, 388
Temazepam, as premedicant, 430–431
  pharmacologic properties of, 429–431
Tetrodotoxin (TTX), pharmacologic properties of, 366
Thermodilution cardiac output, principles of, 756–763
Thermodilution technique, for monitoring right ventricular function, 855–856
Thiopental, effects of, on coronary blood flow, 608
Thiorphan, for analgesia in cancer patients, 330–331
Thoracic electrical impedance, in measurement of cardiac output, 819–820
Thrombocytopenia, critical care drugs associated with, in multisystem failure, 26
  factors leading to, in multisystem failure, 25–26
Thrombolytic therapy, for treatment of acute myocardial infarction, 635–637
Thrombotic thrombocytopenic purpura (TTP), and coagulation disorders, 31–32
Tocolytics, in obstetrics, 450–451
Total parenteral nutrition, for patients in hemorrhagic shock, 125–126
Transcutaneous oxygen monitoring, in pediatric cardiac monitoring, 829
Transplantation, of liver, and coagulopathy, 31–32
Triazolam, as premedicant, 433–434
  pharmacologic properties of, 431–434
Two-dimensional echocardiography, for monitoring right ventricular function, 855
  in pediatric cardiac monitoring, and color flow Doppler, 833–834

Ulcers, stress, of stomach, role of, and multisystem organ failure, 186–189
Ultrasound, in examination of heart, **769–783**
  in measurement of cardiac output, 819

Valvular function, Doppler evaluation of, 795–799
Vasoconstrictors, for treatment of myocardial ischemia, 581–583
VCO_2 measurement, interpretation of, in critically ill patients, 44–45
Vecuronium, pharmacologic properties of, 343–346
Vecuronium infusion, 342
Venous drainage, of heart, anatomy of, 840
Ventilation, effect of amino acids on, in acutely ill patients, 64–66
Ventricular filling pressure, in diagnosis of myocardial ischemia, 508–509
Ventricular function, global, M-mode for evaluation of, 772–775
    two-dimensional echocardiography for evaluation of, 775–776
  regional, two-dimensional echocardiography for evaluation of, 776–779
Ventricular septal defects, Doppler echocardiography for detection of, 799
Verapamil, for treatment of myocardial ischemia, 578–581
Vitamin K deficiency, as cause of bleeding abnormalities, in multisystem failure, 28–29
Vo_2 measurement, interpretation of, in critically ill patients, 44–45

Wall motion, regional, abnormalities of, development of, following onset of myocardial ischemia, 559–561
    and reperfusion, 561–562

U.S. Postal Service

STATEMENT OF OWNERSHIP, MANAGEMENT AND CIRCULATION

Required by 39 U.S.C. 3685)

1A. TITLE OF PUBLICATION
ANESTHESIOLOGY CLINICS OF NORTH AMERICA

1B. PUBLICATION NO.
0 8 8 9 8 5 3 7

2. DATE OF FILING
7-31-88

3. FREQUENCY OF ISSUE
FOUR ISSUES PER YEAR (MAR, JUNE, SEP, DEC.)

3A. NO. OF ISSUES PUBLISHED ANNUALLY
FOUR

3B. ANNUAL SUBSCRIPTION PRICE
65.00

4. COMPLETE MAILING ADDRESS OF KNOWN OFFICE OF PUBLICATION *(Street, City, County, State and ZIP+4 Code) (Not printers)*
CURTIS CENTER INDEPENDENCE SQUARE WEST, PHILA. PA, 19106-3399

5. COMPLETE MAILING ADDRESS OF THE HEADQUARTERS OF GENERAL BUSINESS OFFICES OF THE PUBLISHER *(Not printer)*
CURTIS CENTER INDEPENDENCE SQUARE WEST, PHILA. PA, 19106-3399

6. FULL NAMES AND COMPLETE MAILING ADDRESS OF PUBLISHER, EDITOR, AND MANAGING EDITOR *(This item MUST NOT be blank)*

PUBLISHER *(Name and Complete Mailing Address)*
W.B. SAUNDERS COMPANY
JOAN BLUMBERG, CURTIS CENTER INDEP SQ. W. PHILADELPHIA PA 19106-3399

EDITOR *(Name and Complete Mailing Address)*
W.B. SAUNDERS COMPANY
MARGARET BURNS, CURTIS CENTER INDEP SQ. W. PHILADELPHIA PA 19106-3399

MANAGING EDITOR *(Name and Complete Mailing Address)*
BARBARA COHEN - KLIGERMAN
CURTIS CENTER INDEPENDENCE SQ. WEST PHILADELPHIA PA 19106-3399

7. OWNER *(If owned by a corporation, its name and address must be stated and also immediately thereunder the names and addresses of stockholders owning or holding 1 percent or more of total amount of stock. If not owned by a corporation, the names and addresses of the individual owners must be given. If owned by a partnership or other unincorporated firm, its name and address, as well as that of each individual must be given. If the publication is published by a nonprofit organization, its name and address must be stated.) (Item must be completed.)*

FULL NAME	COMPLETE MAILING ADDRESS
W.B. SAUNDERS, INC. STOCK IS	
OWNED 100% BY HARCOURT BRACE	
JOVANOVICH INC.	

8. KNOWN BONDHOLDERS, MORTGAGEES, AND OTHER SECURITY HOLDERS OWNING OR HOLDING 1 PERCENT OR MORE OF TOTAL AMOUNT OF BONDS, MORTGAGES OR OTHER SECURITIES *(If there are none, so state)*

FULL NAME	COMPLETE MAILING ADDRESS
NONE	

9. FOR COMPLETION BY NONPROFIT ORGANIZATIONS AUTHORIZED TO MAIL AT SPECIAL RATES *(Section 423.12 DMM only)*
The purpose, function, and nonprofit status of this organization and the exempt status for Federal income tax purposes *(Check one)*

(1) ☐ HAS NOT CHANGED DURING PRECEDING 12 MONTHS
(2) ☐ HAS CHANGED DURING PRECEDING 12 MONTHS
(If changed, publisher must submit explanation of change with this statement.)

10. EXTENT AND NATURE OF CIRCULATION *(See instructions on reverse side)*	AVERAGE NO. COPIES EACH ISSUE DURING PRECEDING 12 MONTHS	ACTUAL NO. COPIES OF SINGLE ISSUE PUBLISHED NEAREST TO FILING DATE
A. TOTAL NO. COPIES *(Net Press Run)*	5,000	5,000
B. PAID AND/OR REQUESTED CIRCULATION 1. Sales through dealers and carriers, street vendors and counter sales		
2. Mail Subscription *(Paid and/or requested)*	2,887	2,901
C. TOTAL PAID AND/OR REQUESTED CIRCULATION *(Sum of 10B1 and 10B2)*	2,887	2,901
D. FREE DISTRIBUTION BY MAIL, CARRIER OR OTHER MEANS SAMPLES, COMPLIMENTARY, AND OTHER FREE COPIES	76	76
E. TOTAL DISTRIBUTION *(Sum of C and D)*	2,963	2,977
F. COPIES NOT DISTRIBUTED 1. Office use, left over, unaccounted, spoiled after printing	2,037	2,023
2. Return from News Agents		
G. TOTAL *(Sum of E, F1 and 2—should equal net press run shown in A)*	5,000	5,000

11. I certify that the statements made by me above are correct and complete

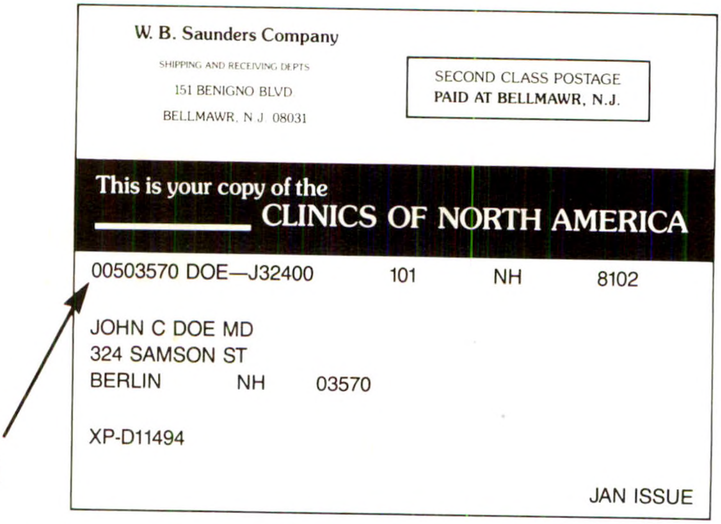
SIGNATURE AND TITLE OF EDITOR, PUBLISHER, BUSINESS MANAGER, OR OWNER
Lisa Kennedy, Business Manager

PS Form 3526, Dec. 1985 *(See instruction on reverse)*

Changing Your Address?

Make sure your subscription changes too! When you notify us of your new address, you can help make our job easier by including an exact copy of your Clinics label number with your old address (see illustration below.) This number identifies you to our computer system and will speed the processing of your address change. Please be sure this label number accompanies your old address and your corrected address—you can send an old Clinics label with your number on it or just copy it exactly and send it to the address listed below.

We appreciate your help in our attempt to give you continuous coverage. Thank you.



W. B. Saunders Company
SHIPPING AND RECEIVING DEPTS
151 BENIGNO BLVD
BELLMAWR, N.J. 08031

SECOND CLASS POSTAGE
PAID AT BELLMAWR, N.J.

This is your copy of the
__________ CLINICS OF NORTH AMERICA

00503570 DOE—J32400 101 NH 8102

JOHN C DOE MD
324 SAMSON ST
BERLIN NH 03570

XP-D11494

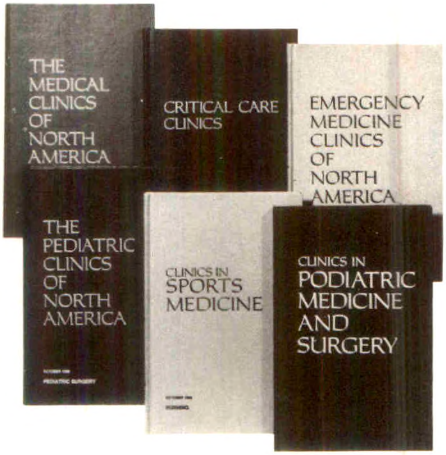
JAN ISSUE

Your Clinics Label Number

Copy it exactly or send your label along with your address to:
W. B. Saunders Company, Fulfillment Services
The Curtis Center
Independence Square West, Philadelphia, PA 19106-3399.

Please allow four to six weeks for delivery of new subscriptions and for processing address changes.

WHATEVER YOUR SPECIALTY— SAUNDERS CLINICS KEEP YOU CURRENT!


THE MEDICAL CLINICS OF NORTH AMERICA
CRITICAL CARE CLINICS
EMERGENCY MEDICINE CLINICS OF NORTH AMERICA
THE PEDIATRIC CLINICS OF NORTH AMERICA
CLINICS IN SPORTS MEDICINE
CLINICS IN PODIATRIC MEDICINE AND SURGERY

SUBSCRIBE TODAY!

These unique periodicals from Saunders are a sure way to keep current in your specialty, with the up-to-date information you need in a durable, hard-cover format. Every issue of the Clinics is devoted to a topic of current concern in your field and written by leading authorities. A subscription to the Clinics guarantees you won't miss one important issue—and will save you money over the single issue price.

Subscribe now to the Clinics of your choice and get the concise, current, and thoroughly practice-applicable know-how you need. You'll receive your first volume for a 30-day, no-obligation review. If you are not completely satisfied, simply write "Cancel my subscription" on the invoice, return it and owe nothing. To order, fill out the card below, tear it off, and drop it in the mail today!

Changing your address? Please notify us promptly so your subscription can continue uninterrupted. If available, submit your Clinics mailing label with your address change or copy your Clinics label number exactly in the space provided below. Please allow 4 to 6 weeks for delivery of new subscriptions and for processing of address changes.

SUBSCRIBE TODAY! DETACH AND MAIL THIS NO-RISK CARD TODAY!

YES! Please start my subscription to the Clinics checked below with the current issue, and continue my subscription at the then current price until I notify you otherwise. If not completely satisfied with my first issue I may write "cancel" on the invoice and return it within 30 days at no further obligation.

☐ Bill me ☐ Check enclosed ☐ VISA ☐ MasterCard

card # ____/____/____/____exp. __/__

Signature________________

This is not a renewal notice. Add sales tax where applicable.

Clinics

☐ Medical Clinics
Bimonthly, $55.00
Institutions, $64.00

☐ Anesthesiology
Quarterly, $65.00
Institutions, $75.00

☐ Cardiology
Quarterly, $65.00
Institutions, $75.00

☐ Chest Medicine
Quarterly, $66.00
Institutions, $75.00

☐ Critical Care
Quarterly, $60.00
Institutions, $70.00

☐ Dental Clinics
Quarterly, $56.00
Institutions, $65.00

☐ Dermatologic
Quarterly, $75.00
Institutions, $85.00

☐ Emergency Medicine
Quarterly, $60.00
Institutions, $70.00

☐ Endocrinology & Metabolism
Quarterly, $66.00
Institutions, $75.00

☐ Gastroenterology
Quarterly, $65.00
Institutions, $75.00

☐ Geriatric Medicine
Quarterly, $59.00
Institutions, $70.00

☐ Hand Clinics
Quarterly, $76.00
Institutions, $85.00

☐ Hematology/Oncology
Quarterly, $65.00
Institutions, $75.00

☐ Immunology & Allergy
3 times yearly, $57.00
Institutions, $70.00

☐ Infectious Disease
Quarterly, $59.00
Institutions, $70.00

☐ Laboratory Medicine
Quarterly, $55.00
Institutions, $64.00

☐ Neurologic
Quarterly, $66.00
Institutions, $75.00

☐ Nursing Clinics
Quarterly, $39.00
Institutions, $45.00

☐ Obstetrics & Gynecology
Quarterly, $65.00
Institutions, $75.00

☐ Orthopedic Clinics
Quarterly, $66.00
Institutions, $75.00

☐ Otolaryngologic
Quarterly, $72.00
Institutions, $83.00

☐ Pediatric
Bimonthly, $53.00
Institutions, $62.00

☐ Perinatology
Quarterly, $56.00
Institutions, $65.00

☐ Plastic Surgery
Quarterly, $89.00
Institutions, $102.00

☐ Podiatric Medicine & Surgery
Quarterly, $61.00
Institutions, $72.00

☐ Primary Care
Quarterly, $53.00
Institutions, $62.00

☐ Psychiatric
Quarterly, $65.00
Institutions, $75.00

☐ Radiologic
Bimonthly, $89.00
Institutions, $102.00

☐ Rheumatic Disease
3 times yearly, $57.00
Institutions, $70.00

☐ Sports Medicine
Quarterly, $62.00
Institutions, $72.00

☐ Surgical Clinics
Bimonthly, $68.00
Institutions, $78.00

☐ Urologic Clinics
Quarterly, $72.00
Institutions, $83.00

☐ Veterinary: Small Animal Practice
Bimontly, $66.00
Institutions, $75.00

☐ Veterinary: Equine Practice
3 times yearly, $54.00
Institutions, $62.00

Please Print:

Name________________
Address________________
City________________
State________________Zip________

☐ Veterinary: Food Animal Practice
3 times yearly, $43.00
Institutions, $50.00

Journals

☐ The American Journal of Emergency Medicine
Vol 6 (6 issues), 1988
Individuals: $62.00,
Residents: $42.00,
Institutions: $82.00

☐ American Journal of Otolaryngology
Vol 9 (6 issues), 1988
Individuals: $60.00,
Residents: $38.00,
Institutions: $78.00

☐ Human Pathology
Vol 19 (12 issues), 1988
Individuals: $80.00,
Residents: $50.00,
Institutions: $96.00

☐ Journal of Oral and Maxillofacial Surgery
Vol 46 (12 issues), 1988
Individuals: $60.00,
Residents: $45.00,
Institutions: $70.00

☐ Journal of Perinatology
Vol 8 (4 issues), 1988
Individuals: $39.00,
Residents: $30.00,
Institutions: $65.00

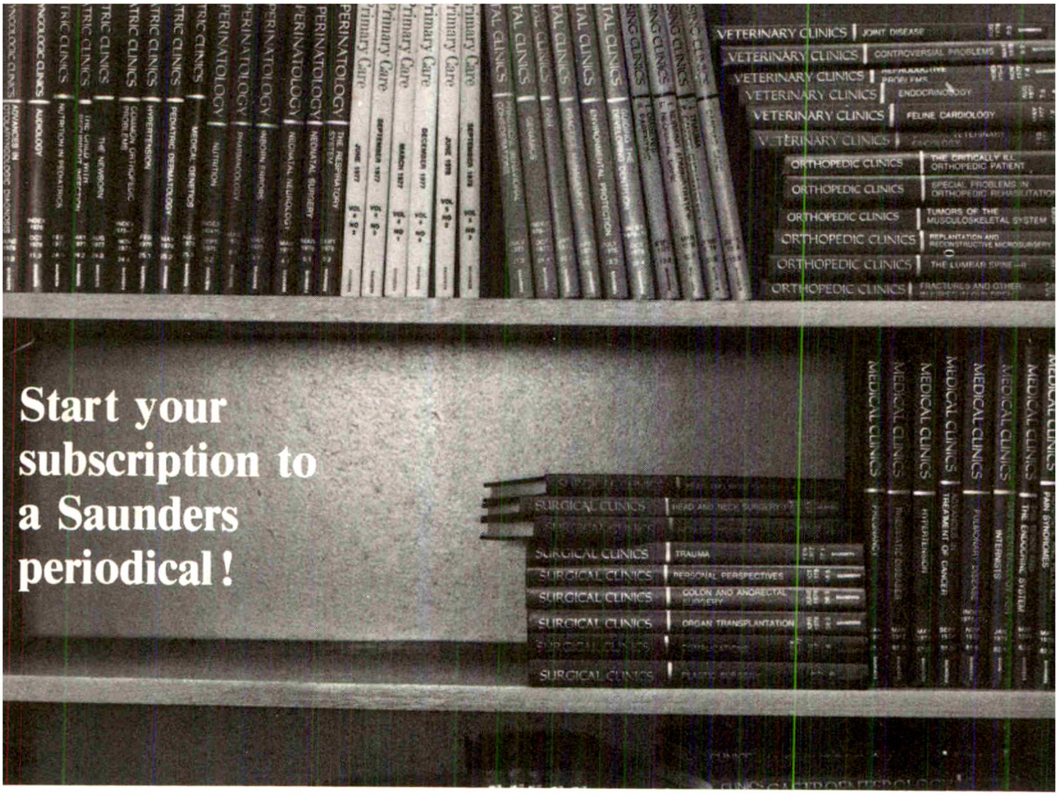
☐ Journal of Professional Nursing
Vol 4 (6 issues), 1988
Individuals: $49.00,
Students: $35.00,
Institutions: $75.00

CHANGE OF ADDRESS

Label No.________________
Old address________________
City________________
State________________Zip________
Effective________________
Send to new address above.

Printed in USA. Prices US only and subject to change without notice.

mo10245



Order your subscription today. Simply complete and detach the card below and drop it in the mail to receive the best clinical information in your field.

NO POSTAGE
NECESSARY
IF MAILED
IN THE
UNITED STATES

BUSINESS REPLY MAIL
FIRST CLASS PERMIT NO. 101 PHILADELPHIA, PA

POSTAGE WILL BE PAID BY ADDRESSEE

W. B. SAUNDERS
Harcourt Brace Jovanovich, Inc.
West Washington Square
Philadelphia, PA 19105-9967